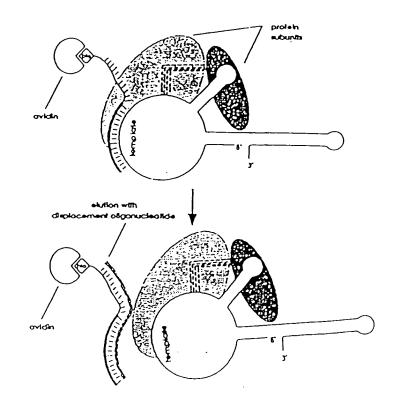
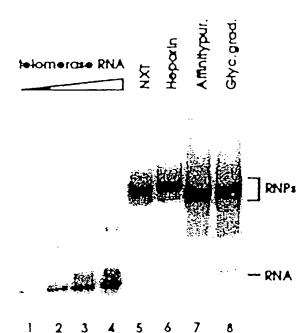
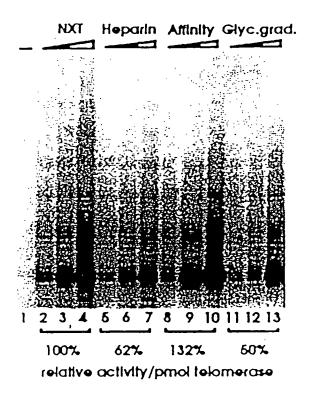
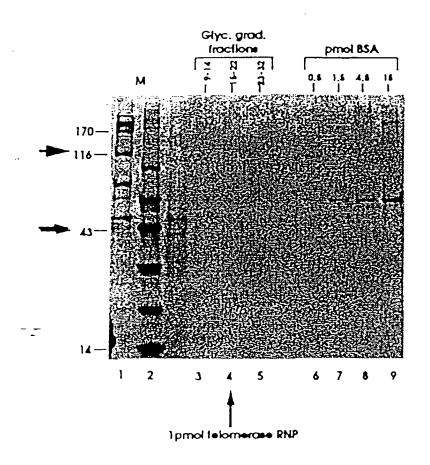
PANEL A

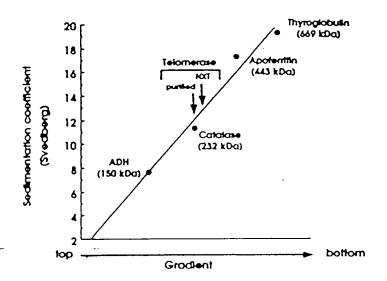
PANEL B

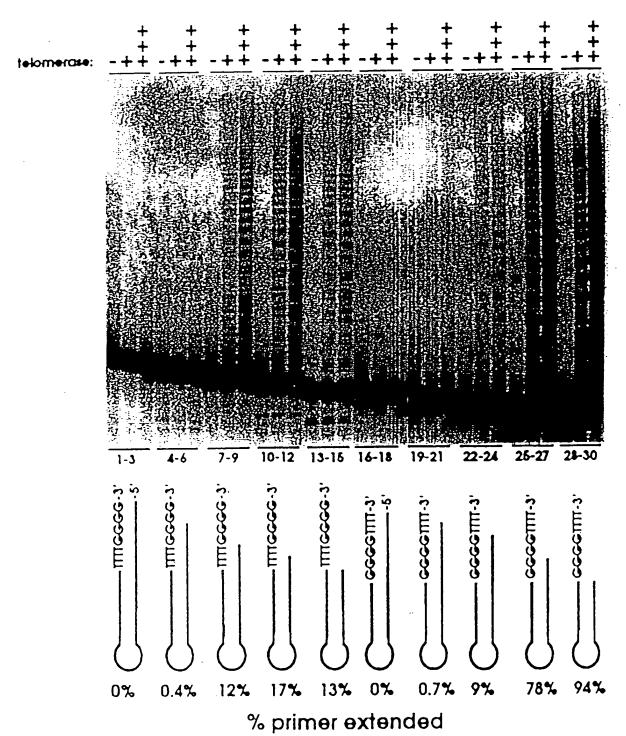


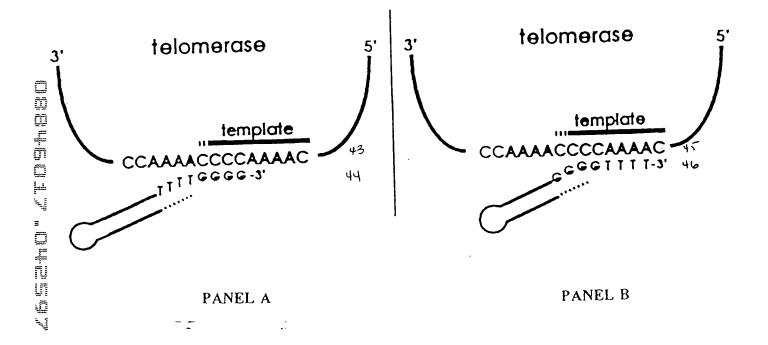


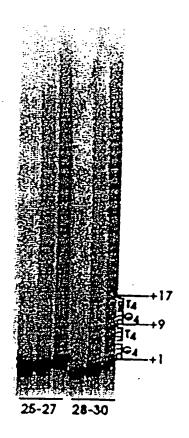












1 AAAACCCCAA AACCCCAAAA CCCCTTTTAG AGCCCTGCAG TTGGAAATAT 51 AACCTCAGTA TTAATAAGCT CAGATTTTAA ATATTAATTA CAAAACCTAA 101 ATGGAGGTTG ATGTTGATAA TCAAGCTGAT AATCATGGCA TTCACTCAGC 151 TCTTAAGACT TGTGAAGAAA TTAAAGAAGC TAAAACGTTG TACTCTTGGA 201 TCCAGAAAGT TATTAGATGA AGAAATCAAT CTCAAAGTCA TTATAAAGAT 251 TTAGAAGATA TTAAAATATT TGCGCAGACA AATATTGTTG CTACTCCACG 301 AGACTATAAT GAAGAAGATT TTAAAGTTAT TGCAAGAAAA GAAGTATTTT 351 CAACTGGACT AATGATCGAA CTTATTGACA AATGCTTAGT TGAACTTCTT 401 TCATCAAGCG ATGTTTCAGA TAGACAAAAA CTTCAATGAT TTGGATTTCA 451 ACTTAAGGGA AATCAATTAG CAAAGACCCA TTTATTAACA GCTCTTTCAA 501 CTCAAAAGCA GTATTTCTTT CAAGACGAAT GGAACCAAGT TAGAGCAATG 551 ATTGGAAATG AGCTCTTCCG ACATCTCTAC ACTAAATATT TAATATTCCA 601 GCGAACTTCT GAAGGAACTC TTGTTCAATT TTGCGGGAAT AACGTTTTTG 651 ATCATTTGAA AGTCAACGAT AAGTTTGACA AAAAGCAAAA AGGTGGAGCA 701 GCAGACATGA ATGAACCTCG ATGTTGATCA ACCTGCAAAT ACAATGTCAA 751 GAATGAGAAA GATCACTTTC TCAACAACAT CAACGTGCCG AATTGGAATA 801 ATATGAAATC AAGAACCAGA ATATTTTATT GCACTCATTT TAATAGAAAT 851 AACCAATTCT TCAAAAAGCA TGAGTTTGTG AGTAACAAAA ACAATATTTC 901 AGCGATGGAC AGAGCTCAGA CGATATTCAC GAATATATTC AGATTTAATA 951 GAATTAGAAA GAAGCTAAAA GATAAGGTTA TCGAAAAAAT TGCCTACATG 1001 CTTGAGAAAG TCAAAGATTT TAACTTCAAC TACTATTTAA CAAAATCTTG 1051 TCCTCTTCCA GAAAATTGGC GGGAACGGAA ACAAAAAATC GAAAACTTGA 1101 TAAATAAAC TAGAGAAGAA AAGTCGAAGT ACTATGAAGA GCTGTTTAGC 1151 TACACAACTG ATAATAAATG CGTCACACAA TTTATTAATG AATTTTTCTA 1201 CAATATACTC CCCAAAGACT TTTTGACTGG AAGAAACCGT AAGAATTTTC 1251 AAAAGAAAGT TAAGAAATAT GTGGAACTAA ACAAGCATGA ACTCATTCAC 1301 AAAAACTTAT TGCTTGAGAA GATCAATACA AGAGAAATAT CATGGATGCA 1351 GGTTGAGACC TCTGCAAAGC ATTTTTATTA TTTTGATCAC GAAAACATCT 1401 ACGTCTTATG GAAATTGCTC CGATGGATAT TCGAGGATCT CGTCGTCTCG 1451 CTGATTAGAT GATTTTTCTA TGTCACCGAG CAACAGAAAA GTTACTCCAA 1501 AACCTATTAC TACAGAAAGA ATATTTGGGA CGTCATTATG AAAATGTCAA 1551 TCGCAGACTT AAAGAAGGAA ACGCTTGCTG AGGTCCAAGA AAAAGAGGTT 1601 GAAGAATGGA AAAAGTCGCT TGGATTTGCA CCTGGAAAAC TCAGACTAAT 1651 ACCGAAGAAA ACTACTTTCC GTCCAATTAT GACTTTCAAT AAGAAGATTG 1701 TAAATTCAGA CCGGAAGACT ACAAAATTAA CTACAAATAC GAAGTTATTG 1751 AACTCTCACT TAATGCTTAA GACATTGAAG AATAGAATGT TTAAAGATCC 1801 TTTTGGATTC GCTGTTTTTA ACTATGATGA TGTAATGAAA AAGTATGAGG 1851 AGTTTGTTTG CAAATGGAAG CAAGTTGGAC AACCAAAACT CTTCTTTGCA 1901 ACTATGGATA TCGAAAAGTG ATATGATAGT GTAAACAGAG AAAAACTATC 1951 AACATTCCTA AAAACTACTA AATTACTTTC TTCAGATTTC TGGATTATGA 2001 CTGCACAAAT TCTAAAGAGA AAGAATAACA TAGTTATCGA TTCGAAAAAC 2051 TTTAGAAAGA AAGAAATGAA AGATTATTTT AGACAGAAAT TCCAGAAGAT 2101 TGCACTTGAA GGAGGACAAT ATCCAACCTT ATTCAGTGTT CTTGAAAATG 2201 AGAAATTATT TTAAGAAAGA TAACTTACTT CAACCAGTCA TTAATATTTG 2251 CCAATATAAT TACATTAACT TTAATGGGAA GTTTTATAAA CAAACAAAAG 2301 GAATTCCTCA AGGTCTTTGA GTTTCATCAA TTTTGTCATC ATTTTATTAT

### FIGURE 9 (cont.)

2351	GCAACATTAG AGGAAAGCTC CTTAGGATTC CTTAGAGATG AATCAATGAA
2401 <sup>-</sup>	CCCTGAAAAT CCAAATGTTA ATCTTCTAAT GAGACTTACA GATGACTATC
2451	TTTTGATTAC AACTCAAGAG AATAATGCAG TATTGTTTAT TGAGAAACTT
2501	ATAAACGTAA GTCGTGAAAA TGGATTTAAA TTCAATATGA AGAAACTACA
2551	GACTAGTTTT CCATTAAGTC CAAGCAAATT TGCAAAATAC GGAATGGATA
2601	GTGTTGAGGA GCAAAATATT GTTCAAGATT ACTGCGATTG GATTGGCATC
2651	TCAATTGATA TGAAAACTCT TGCTTTAATG CCAAATATTA ACTTGAGAAT
2701	AGAAGGAATT CTGTGTACAC TCAATCTAAA CATGCAAACA AAGAAAGCAT
2751	CAATGTGGCT CAAGAAGAAA CTAAAGTCGT TTTTAATGAA TAACATTACC
2801	CATTATTTTA GAAAGACGAT TACAACCGAA GACTTTGCGA ATAAAACTCT
2851	CAACAAGTTA TTTATATCAG GCGGTTACAA ATACATGCAA TGAGCCAAAG
2901	AATACAAGGA CCACTTTAAG AAGAACTTAG CTATGAGCAG TATGATCGAC
2951	TTAGAGGTAT CTAAAATTAT ATACTCTGTA ACCAGAGCAT TCTTTAAATA
3001	CCTTGTGTGC AATATTAAGG ATACAATTTT TGGAGAGGAG CATTATCCAG
3051	ACTITITCCT TAGCACACTG AAGCACTTTA TTGAAATATT CAGCACAAAA
3101	AAGTACATTT TCAACAGAGT TTGCATGATC CTCAAGGCAA AAGAAGCAAA
3151	GCTAAAAAGT GACCAATGTC AATCTCTAAT TCAATATGAT GCATAGTCGA
3201	CTATTCTAAC TTATTTTGGA AAGTTAATTT TCAATTTTTG TCTTATATAC

3251 TGGGGTTTTG GGGTTTTGGG GTTTTGGGG

- 1 MEVDVDNQAD NHGIHSALKT CEEIKEAKTL YSWIQKVIRC RNQSQSHYKD
- 51 LEDIKIFAQT NIVATPRDYN EEDFKVIARK EVFSTGLMIE LIDKCLVELL
- 101 SSSDVSDRQK LQCFGFQLKG NQLAKTHLLT ALSTQKQYFF QDEWNQVRAM
- 151 IGNELFRHLY TKYLIFORTS EGTLVOFCGN NVFDHLKVND KFDKKQKGGA
- 201 ADMNEPRCCS TCKYNVKNEK DHFLNNINVP NWNNMKSRTR IFYCTHFNRN
- 251 NOFFKKHEFV SNKNNISAMD RAQTIFTNIF RFNRIRKKLK DKVIEKIAYM
- 301 LEKVKDFNFN YYLTKSCPLP ENWRERKQKI ENLINKTREE KSKYYEELFS
- 351 YTTDNKCVTQ FINEFFYNIL PKDFLTGRNR KNFQKKVKKY VELNKHELIH
- 401 KNLLLEKINT REISWMOVET SAKHFYYFDH ENIYVLWKLL RWIFEDLVVS
- 451 LIRCFFYVTE QQKSYSKTYY YRKNIWDVIM KMSIADLKKE TLAEVQEKEV
- 501 EEWKKSLGFA PGKLRLIPKK TTFRPIMTFN KKIVNSDRKT TKLTTNTKLL
- 551 NSHLMLKTLK NRMFKDPFGF AVFNYDDVMK KYEEFVCKWK QVGQPKLFFA
- 601 TMDIEKCYDS VNREKLSTFL KTTKLLSSDF WIMTAQILKR KNNIVIDSKN
- 651 FRKKEMKDYF ROKFOKIALE GGOYPTLFSV LENEQNDLNA KKTLIVEAKQ
- 701 RNYFKKDNLL QPVINICQYN YINFNGKFYK QTKGIPQGLC VSSILSSFYY
- 751 ATLEESSLGF LRDESMNPEN PNVNLLMRLT DDYLLITTQE NNAVLFIEKL
- 801 INVSRENGFK FNMKKLQTSF PLSPSKFAKY GMDSVEEQNI VQDYCDWIGI
- 851 SIDMKTLALM PNINLRIEGI LCTLNLNMQT KKASMWLKKK LKSFLMNNIT
- 901 HYFRKTITTE DFANKTLNKL FISGGYKYMQ CAKEYKDHFK KNLAMSSMID
- 951 LEVSKIIYSV TRAFFKYLVC NIKDTIFGEE HYPDFFLSTL KHFIEIFSTK
- 1001 KYIFNRVCMI LKAKEAKLKS DQCQSLIQYD A

1751 GGGGTTTTGG GG

1	CCCCAAAACC CCAAAACCCC AAAACCCCTA TAAAAAAAGA AAAAATTGAG
51	GTAGTTTAGA AATAAAATAT TATTCCCGCA CAAATGGAGA TGGATATTGA
101	TTTGGATGAT ATAGAAAATT TACTTCCTAA TACATTCAAC AAGTATAGCA
151	GCTCTTGTAG TGACAAGAAA GGATGCAAAA CATTGAAATC TGGCTCGAAA
201	TCGCCTTCAT TGACTATTCC AAAGTTGCAA AAACAATTAG AGTTCTACTT
251	CTCGGATGCA AATCTTTATA ACGATTCTTT CTTGAGAAAA TTAGTTTTAA
301	AAAGCGGAGA GCAAAGAGTA GAAATTGAAA CATTACTAAT GTTTAAATAA
351	AATCAGGTAA TGAGGATTAT TCTATTTTTT AGATCACTTC TTAAGGAGCA
401	TTATGGAGAA AATTACTTAA TACTAAAAGG TAAACAGTTT GGATTATTTC
451	CCTAGCCAAC AATGATGAGT ATATTAAATT CATATGAGAA TGAGTCAAAG
501	GATCTCGATA CATCAGACTT ACCAAAGACA AACTCGCTAT AAAACGCAAG
551	AAAAAGTTTG ATAATCGAAC AGCAGAAGAA CTTATTGCAT TTACTATTCG
601	TATGGGTTTT ATTACAATTG TTTTAGGTAT CGACGGTGAA CTCCCGAGTC
651	TTGAGACAAT TGAAAAAGCT GTTTACAACT GAAGGAATCG CAGTTCTGAA
701	AGTTCTGATG TGTATGCCAT TATTTTGTGA ATTAATCTCA AATATCTTAT
751	CTCAATTTAA TGGATAGCTA TAGAAACAAA CCAAATAAAC CATGCAAGTT
801	TAATGGAATA TACGTTAAAT CCTTTGGGAC AAATGCACAC TGAATTTATA
851	TTGGATTCTT AAAGCATAGA TACACAGAAT GCTTTAGAGA CTGATTTAGC
901	TTACAACAGA TTACCTGTTT TGATTACTCT TGCTCATCTC TTATATCTTT
951	
1001	
1051	
1101	
1151	
1201	
1251	
1301	
1351	
1401	
1451	
1501	
1551	
1601	
1651	
1701	AAGATTTATT TTTTTCAATA ATTTATTGAA AAGAGGGGTT TTGGGGTTTT

	1	0
a b c	PQNPKTPKPL * KKKKLR** FR - PKTPKPQNPYKKRKNCGSLE - PKPQNPKTPIKKEKIEVV*K-	
	AATAAAATATTATTCCCGCACAAATGGAGATGGATATTGGATGTTTGGATGATATAGAAAATT	20
a	TTATTTTATAATAAGGGCGTGTTTACCTCTACCTATAACTAAACCTACTATATCTTTTAA  N K I L F P H K W R W I L I W M I . * K I -	
b c	I K Y Y S R T N G D G Y C F G C Y R K F - N I I P A Q M E M D I D L D D I E N L -	
	TACTTCCTAATACATTCAACAAGTATAGCAGCTCTTGTAGTGACAAGAAAGGATGCAAAA	a r
	ATGAAGGATTATGTAAGTTGTTCATATCGTCGAGAACATCACTGTTCTTTCCTACGTTTT	,
a b c	Y F L I H S T S I A A L V V T R K D A K - T S * Y I Q Q V * Q L L * * Q E R M Q N - L P N T F N K Y S S S C S D K K G C K T -	
	CATTGAAATCTGGCTCGAAATCGCCTTCATTGACTATTCCAAAGTTGCAAAAACAATTAG	
	GTAACTTTAGACCGAGCTTTAGCGGAAGTAACTGATAAGGTTTCAACGTTTTTGTTAATC	10
a b c	H C N L A R N R L H C L F Q S C K N N · - I E I W L E I A F I D Y S K V A K T I R - L K S G S K S P S L T I P K L Q K Q L K -	
	AGTTCTACTTCTCGGATGCAAATCTTTATAACGATTCTTTCT	
	241	0
a b c	S S T S R M Q I F I T I L S C E N · F · · V L L L G C K S L · R F F L E K I S F K - F Y F S D A N L Y N D S F L R K L V L K -	
	AAAGCGGAGAGCAAAGAGTAGAAATTGAAACATTACTAATGTTTAAATAAA	
	301	0
a b c	K A E S K E · K L K H Y · C L N K I R · - K R R A K S R N C N I T N V · I K S G N - S G E Q R V B I E T L L M F K · N Q V M -	
	TGAGGATTATTCTATTTTTTAGATCACTTCTTAAGGAGCATTATGGAGAAAATTACTTAA	_
	ACTCCTAATAAGATAAAAATCTAGTGAAGAATTCCTCGTAATACCTCTTTTAATGAATT	0
a b c	C G L F Y F L D H F L R S I M E K I T * - E D Y S I F * I T S * G A L W R K L L N - R I I L F F R S L L K E H Y G E N Y L I -	
	TACTAAAAGGTAAACAGTTTGGATTATTTCCCTAGCCAACAATGATGAGTATATTAAATT	
	421	0
a b c	Y · K V N S L D Y F P S Q Q C C V Y · I - T K R · T V W I I S L A N N D E Y I K F - L K G X Q F G L F P · P T M M S I L N S -	

### FIGURE 12 (cont.)

		CATATGAGAATGAGTCAAAGGATCTCGATACATCAGACTTACCAAAGACAAACTCGCTAT	540
	481	GTATACTCTACTCAGTTTCCTAGAGCTATGTAGTCTGAATGGTTTCTGTTTGAGCGATA	340
a b c	1	H M R M S Q R I S I H Q T Y Q R Q T R Y I C E C V K G S R Y I R L T K D K L A I Y E N E S K D L D T S D L P K T N S L *	-
	541	AAAACGCAAGAAAAAGTTTGATAATCGAACAGCAGAAGAACTTATTGCATTTACTATTCG TTTTGCGTTCTTTTTCAAACTATTAGCTTGTCGTCTTCTTGAATAACGTAAATGATAAGC	600
a b c	:	KTQEKVC * SNSRRTYCIYYS KRKKFDNRTAEELIAFTIR NARKSLIIEQQKNLLHLLFV	-
	601	TATGGGTTTTATTACAATTGTTTTAGGTATCGACGGTGAACTCCCGAGTCTTGAGACAAT  ATACCCAAAATAATGTTAACAAAATCCATAGCTGCCACTTGAGGGCTCAGAACTCTGTTA	660
a b c	•	Y G F Y Y N C F R Y R R C T P E S C D N M G F I T I V L G I D G E L P S L E T I W V L L Q L F • V S T V N S R V L R Q L	- - -
	661	TGAAAAAGCTGTTTACAACTGAAGGAATCGCAGTTCTGAAAGTTCTGATGTGTATGCCAT ACTTTTTCGACAAATGTTGACTTCCTTAGCGTCAAGACTTCCAAGACTACACATACGGTA	720
a b c	(	C K S C L Q L K E S Q F C K F * C V C H E K A V Y N C R N R S S E S S D V Y A I K K L F T T E G I A V L K V L M C M P L	- - -
	721	TATTTTGTGAATTAATCTCAAATATCTTATCTCAATTTAATGGATAGCTATAGAAACAAA ATAAAACACTTAATTAGAGTTTATAGAATAGA	780
a b c	,	Y F V N · S Q I S Y L N L M D S Y R N K I L C I N L K Y L I S I · W I A I E T N F C E L I S N I L S Q F N G · L · K Q T	- -
	781	CCAAATAAACCATGCAAGTTTAATGGAATATACGTTAAATCCTTTGGGACAAATGCACAC GGTTTATTTGGTACGTTCAAATTACCTTATATGCAATTTAGGAAACCCTGTTTACGTGTG	840
a b c	:	PNKPCKFNGIYVKSFGTNAH QINHASLMEYTLNPLGQMHT KTMQV-WNIR ILWDKCTL	- -
	841	TGAATTTATATTGGATTCTTAAAGCATAGATACACAGAATGCTTTAGAGACTGATTTAGC ACTTAAATATAACCTAAGAATTTCGTATCTATGTGTCTTACGAAATCTCTGACTAAATCG	900
a b c	(	C I Y I G F L K H R Y T E C F R D C F S E F I L D S ' S I D T Q N A L E T D L A N L Y W I L K A * I H R M L' * R L I * L	- -
	901	TTACAACAGATTACCTGTTTTGATTACTCTTGCTCATCTCTTATATCTTTAAAAGAAGCA AATGTTGTCTAATGGACAAAACTAATGAGAACGAGTAGAGAATATAGAAATTTTCTTCGT	960
a b c	i	LQQITCFDYSCSSLISLKEA YNRLPVLITLAHLLYL KKQ TTDYLFCLLLLISYIFKRSR	-
	961	GGCGAAATGAAAGAAGACTAAAGAAAGAGAGATTTCAAAATTTGTTGATTCTTCTGTAACC CCGCTTTACTTTTCTTCTGATTTCTTCTCTAAAGTTTTTAAACAACTAAGAAGACATTGG	1020
a b c	•	G E M K R R L K K E I S K F V D S S V T A K C K E D ' R K R F Q N L L I L L * P R N E K K T K E R D F K I C C F F C N R	
	1021	GGAATTAACAACAAGAATATTAGCAACGAAAAAGAAGAAGAGCTATCACAATCCTGATTC CCTTAATTGTTGTTCTTATAATCGTTGCTTTTTCTTCTTCTCGATAGTGTTAGGACTAAG	1080
a b c	•	G I N N K N I S N E K E E E L S Q S C F E L T T R I L A T K K K K S Y H N P D S N · Q Q E Y · Q R K R R A I T I L I L	- - -

### FIGURE 12 (cont.)

	TTAAAGATTTCAAAAATTCCAGGTAAGAGAGATACATTCATT	140
	1081	140
a b c	L K I S K I P G K R D T F I K I H I L ° - • R F Q K F Q V R E I H S L K F I Y Y S - K D F K N S R • E R Y I H • N S Y I I V -	
	TTTTTCATTTCACAGCTGTTATTTTCTTTATCTTAACAATATTTTTTTGATTAGCTGGAA  1141	200
a b c	FFISQLLFSFILTIFFD * LE - FSFHSCYFLLS * QYFLISWK - FHFTAVIFFYLNNIFCLAGS-	
	GTAAAAAGTATCAAATAAGAGAAGCGCTAGACTGAGGTAACTTAGCTTATTCACATTCAT  1201	260
a b c	V K S I K * E K R * T E V T * L I H I H - * K V S N K R S A R L R * L S L F T F I - K K Y Q I R E A L D C G N L A Y S H S * -	
	AGATCGACCTTCATATATCCAATACGATGATAAGGAAACAGCAGTCATCCGTTTTAAAAA 1261	320
a b c	R S T F I Y P I R C * G N S S H P F * K - D R P S Y I Q Y D D K E T A V I R F K N - I D L H I S N T M I R K Q Q S S V L K I -	
	TAGTGCTATGAGGACTAAATTTTTAGAGTCAAGAAATGGAGCCGAAATCTTAATCAAAAA  1321	380
a b c	· C Y E D · I F R V K K W S R N L N Q K - S A M R T K F L E S R N G A E I L I K K - V L C G L N F · S Q E M E P K S · S K R -	
	GAATTGCGTCGATATTGCAAAAGAATCGAACTCTAAATCTTTCGTTAATAAGTATTACCA 1381 1 CTTAACGCAGCTATAACGTTTTCTTAGCTTGAGATTTAGAAAGCAATTATTCATAATGGT	440
a b c	ELRRYCKRIEL IFR VLP - NCVDIAKESNSKSFVNKYYQ - IASILQKNRTLNLSLISITN-	
	ATCTTGATTGATGAAGAGATTGACGAGGCAACTGCACAGAAGATCATTAAAGAAATAAA  1441 TAGAACTAACTAACTTCTCTAACTGCTCCGTTGACGTGTCTTCTAGTAATTTCTTTATTT	500
a b c	I L I D C R D · R G N C T E D H · R N K - S C L I E E I D E A T A Q K I I K E I K - L D C L K R S L K K · S -	
	GTAACTTTTATTAATTAGAGAATAAACTAAATTACTAATATAGAGATCAGCGATCTTCAA 1501	560
a b c	V T F I N · R I N · I T N I E I S D L Q · · · L L I R E · T K L L I · R S À I F N · · N F Y · L E N K L N Y · Y R D Q R S S I ·	
	TTGACGAAATAAAAGCTGAACTAAAGTTAGACAATAAAAAAATACAAACCTTGGTCAAAAT 1561	620
a b c	LTK·KLN·S·TIKNTNLGQN - CRNKSCTKVRQ·KIQTĿVKI - DEIKAELKLDNKKYKPWSKY-	
	ATTGAGGAAGGAAAAGAAGACCAGTTAGCAAAAGAAAAATAAGGCAATAAATA	680
a b c	I E E G K E D Q L A K E K I R Q · ! K C · L R K E K K T S · Q K K K · G N K · N E · C C R K R P V S K R K N K A I N K M S ·	

### FIGURE 12 (cont.)

	1681	GTA	ACA(	GAA	GT	GAA	-	АТА													_		_	_			174	4.0
	1001	CAT	CT	стт	'CA	CŢŢ		TAT																			17.	•0
a	,	, ç	) i	к	C	R	N	к	R	F	I		F	F	N		N	L		L	к	:	R	G	,	,	-	
ь		Y	R	S	ε	Ε	I	K		) [	L	F	F	5	5	I	1		Y	С		ĸ	Ε		G	F	-	
С		T	ε	ν	'	K	K	•	K	I	Y	F	•	F	Q	•	•	F	]	ſ	Ε	K		R	G	F	-	
		ттс	SGG	TTT	гтс	GGG	ттт	TGG	GG																			
	1741	<b>-</b> -			+-			+		176	52																	
		AAC	CCC	AAA	AAC	CCC	AAA	ACC	CC																			
a	Ĺ	. G		F	W	G	F	G		-																		
b		W	G	F	G	v	L	G		-																		
~		G	V	1.	- (	7.	F '	w		_																		

2 EVDVDNQADNHGIHSALKTCEEIKEAKTLYSWIQKVIRCRNQSQSHYKDL	51
:::: ::: : :   .::  ::     .  19 ELELEMQENQNDIQVRVKIDDPKQYLVNVTAACLLQEGSYYQDK	62
52 EDIKIFAQTNIVATPRDYNEEDFKVIARKEVF.STGLMIELIDKCLVELL :: ::: ::!     .   .	100
63 DERRYIITKALL EVAESDPEFICQLAVYIRNELYIRTTTNYIVAF.	107
101 SSSDVSDRQKLQCFGFQLKGNQLAKTHLLTALSTQKQYFFQDEWNQVRAM .::  : .::  :. : ::	150
108CVVHKNTQPFIEKYFNKAVLLPNDLLEVCEFAQVLYI	144
151 IGNELFRHLYTKYLIFQRTSEGTLVQFCGNNVFDHLKVNDKFDKKQKGGA ::  ::       .:::: :::::::::::::	200
:: ::     .:::::. ::::::::::::::::	181
201 ADMNEPRCCSTCKYNVKNEKDHFLNNINVPNWNNMKSRTRIFYCTHF .::   .::    ::     .	247
182 SEFNEYQLGKYCTES. QRKKTMFRYLSVTNKQKWDQTKKK	220
248 NRNNQFFKKHEFVSNKNNISAMDRAQTIFTNIFRFNRIRKKLKDKVIEKI	297
:::::  : :::::  .:: : : :.::     .  ::   221 RKENLLTKLQAIKESEDKSKRETGDIMNVEDAIKALKPAVMKKI	264
298 AYMLEKVKDFNFNYYLTKSCPLPENWRERKQKIENLINKTREEKSKYYEE	347
::   ::   ::   ::   ::   ::   ::   :	294
348 LFSYTTDNKCVTQFINEFFYNILPKDFLTGRNRKNFQKKVKKYVELNKHE	397
295 LIKFCHISEPKERVYKILGKKYPKTEEEYKAAFGDSASAPFN.PE	338
398 LIHKNLLLEKINTREISWMQVETSAKHFYYFDHENIYVLWKLLRWIFEDL	447
339 LAGKRMKIEISKTWENELSAKGNTAEVWDNLISSNQLPYMAMLRNLSN	386
448 VVSLIRCFFYVTEQQKSYSKTYYYRKNIWDVIMKMSIADLKKETLAEVQE	497
387ILKAGVSD	394
498 KEVEEWKKSLGFAPGKLRLIPKKTTFRPIMTFNKKIVNSDRKTTKLTTNT	547
395	398
548 KLLNSHLMLKTLKNRMFKDPFGFAVFNYDDVMKKYEEFVCKWKQVGQPKL ::   .   .   .   .   .   .   .   .   .	597
399 IVINKICEPKAVENSKM	415
598 FFATMDIEKCYDSVNREKLSTFLKTTKLLSSDFWIMTAQILKRKNNIVID   1.:t::     1.:v:     1::	547
	457
548 SKNFRKKEMKDYFROKFOKIALEGGOYPTLFSVLENEQNDLNAKKTLIVE	597
458 KTDEEKKDMELEQTEEGEFVKVNEGIGKQYINSIELAIX	496
698 AKQRNYFKKDNLLQPVINICQYNYINFNGKFYKOTKGIPQGLCVSSILSS	
497 IAVNKNLDEIKCHTAIFSDVSGSMSTSMSGGAKKYGSVRTCLECALVLGL	546
748 FYYATLEESSLGFLRDESMNPENPNVNLLMRLTDDYLLITTQENNAVLFI : .       : : : .   . : : : : : : : : :	797
547 MVKQRCEKSSFYIFSSPSSQCNKCYLEVDL	576
798 EKLINVSRENGFKFNMKK.LQTSFPLSPSKFAKYGMDSVEEQNIVQDYCD .:::::	
847 WIGISIDMKTLALMPNINLRIEGILCTLNLNMQTKKASMWLKKKLKSFLM	896
897 NNITHYFRKTITTEDFANKTLNKLFISGGYKYMOCAKEYKD.HFKKNLAM   .:  :::  :::   :::  654 PNIKIFAVDLEGYGKCLNLGDEFNENNYIKIFGM	945
946 SSMIDLEVSKIIYSVTRAFFKYLVCNIKDTIFGEEHYPDFFLSTLKHFIE	995
•	706
996 IFSTKKYIFNRVC 1008	

132	LSTQKQYFFQDEWNQVRAMIGNEL.FRHLYTKYLIFQRTSEGTLVQFC :	178 43
179	GNNVFDHLKVNDKFDKKQKGGAADMNEPRCCSTCKYNVKNEKDHFLNNIN	228
44	:: :.   : :         . ::   KEEDLKLLKFKNQDQDGNSGNDDDDEENNSNKQQELLRRVN	84
229	VPNWNNMKSRTRIFYCTHFNRNNQFFKKHEFVSNKNNISAMDRAQTIFTN	278
85		114
279	IFRFNRIRKKLKDKVIEKIAYMLEKVKDFNFNYYLTKSCPLPENWRERKQ	328
115	GLSEQQVKEEQLRTITEEQVKYQNLVFNMDYQLDLNESGGHRRHRRETDY	164
329	KIENLINKTREEKSKYYEELFSYTTONKCVTOFINE.FFYNILPKDFLTG	377
165	DTEKWFEISHDQK	200
378	RNRKNFQKKVKKYVELNKHELIHKNLLLEKINTREISWMQVETSAKHFYY	427
201	NNYDHLNVSINRLE. TEAEFYAFDDFSQTIKLTNNSYQTVNID	242
428	FDHENIYVLWKLLRWIFEDLVVSLIRCFFYVTEQQKSYSKTYYYRKNI .: :  ::       : :     : :	475
243	VNFDNNLCILALLRFLLSLERFNILNIRSSY. TRNQYNFEKIGELLETI	290
476	WDVIMKMSIADLKKETLAEVQEKEVEEWKKSLGFAPGKLRLIPKKTTFRP	525
291	FAVVFSHR HLQGIHLQVPCEAFQYLVNSSSQISVKDSQLQ	330
526	IMTFNKKIVNSDRKTTKLTTNTKLLNSHLMLKTLKNRMFKDPFGFAVFNY	575
331	VYSFSTDLKLVD. TNKVQDYFKFLQEFPRLTHVSQQAIPVSATNAVENL	378
576	DDVMKKYEEFVCKWKQVGQPKLFFATMDIEKCYDSVNREK :::   :	615
379	NVLLKKVKH. ANLNLVSIPTQFNFDFYFVNLQHLKLEFGLEPNILTKQK	426
616	LSTFLXTTKLLSSDFWIMTAQILKRKNNIVIDSKNFRKKEMK	657
427	LENLLLSIKQSKNLKFLRLNFYTYVAQETSRKQILKQATTIKNLKNNKNQ	476
558	DYFROKFOKIALEGGGYPTLFSVLENEQNDLNAKKTLIVEAKQRNYFK	705
477	EETPETKDETPSESTSGMKFFDHLSELTELEDFSVNLQATQEIY	520
706	KDNELOPVINICQYNYINFNGKFYKQTKGIPQGLCVSSILSSFYYATLEE	755
521	.DSLHKLLIRSTNLKKFKLSYKYEMEKSKMDTFIDLKNIYETLNN	564
756	SSLGFLRDESMNPENPNVNLLMRLTDDYLLITTQENNAVLFIEKLINVSR	805
565	LKRCSVNISNPHGNISYELTNKDSTFYKFKLTLNQE	600
806	ENGFKFNMKKLQTSFPLSPSKFAKYGMDSVEEQNIVQDYCDWIGISIDMK	855
601	LQHAKYTFK QNEFQFNNVKSAKIESSSLESLEDIDSLCKSIASCKNLQ	648
856	TLALMPNINLRIEGILCTLNLNMQT. KKASMWLKK. KLKSFLMNNITH	901
649	NVNI IASLLYPNNIQKNPFNKPNLLFFKQFEQLKNLENVSINC	691
902	YFRKTITTEDFANKTLNKLFISGGYKYMQCAKEYKDHFKKNLAMSSM	948
692	ILDQHILNSISEFLEKNKKIKAFILKRYYLLQYYLDYTKLFKTLQQLPEL	741
949	IDLEVSKIIYSVTRAFFKYLVCNIKDTIFGEEHY	982
742	NQVYINQQLEELTVSEVHKQVWENHKQKAFYEPLCEFIKESSQTLQLIDF	791
983	PDFFLS: TERM TET START:	1028
792	DONTVSDDSIKKILESISESKYHHYLRLNPSQSSSLIKSENEEIQELLK	840

4	DIDLDDIENLLPNTFNKYSSSCSDKKGCKTLKSGSKSPSLTIPK	47
517	::  . ::::    :  .  :  . . NVKSAKIESSSLESLEDIDSLCKSIASCKNLQNVNIIASLLYPNNIQKNP	666
48	LQKQLEFYFSDANLYNDSFLRKLVLKSGEQRVEIETLLM :     :    : :::     :	86
67	FNKPNLLFFKQFEQLKNLENVSINCILDOHILNSISEFLEKNKKIKAFIL	716

	MEMDIDLDDIENL LPNTFNKYSSSCSDKKGCKTLKSGSKSPS	42
491	: :. .:.   :	540
43	LTIPKLOKO LEFYFSDANLYNDSFLRKLVLKSGEORVEIETLL	85
	ALM CLANYOPCERSERVIESS DESCRINCY FUNL PCDE LRPSMOKIL	589

# 

# FIGURE 17

### Motif A

### Motif B

PAIFOSSMTKILEPFRKON SILSSFYYATLEESSLGFL PUMECLALNPLSHQLHNDR PALCNAVLLRLORRLAGLA 3A ? I VD LVYDDL LEFY SEPK LKCKKSVTVIDVGDAYFSVPLDEDFRKYTAFTIP- 7-GIRYQYNVLP<mark>VE</mark>WKG VLPELYFMKFDVKSCYDSIPRMECMRILKDALKN- 68-KCYIREDGLFPESSU 26-HVPVGPRVCV telomerase p123 GQPKLFPATMEIEKCYDSVNREKLSTFLKTTKLL-100-KFYKQTKGIF 28-RQIAIKKGIY KNRNLHCTY IDYKKAEDS I PHSWLIQVLEIYKIN-FGGSNWFREVELKKCFDT I SHDLI I KELKRY I SDч--ч---ч<mark>а</mark>ч--ч al S.c.(groupII)FGGSNWFREW L8543.12 years Dong (LINE) Consensus HIV-RT

### Motif C

## Motif D

### Motif B

4 - ETPARFLOYNI P-PIQ TVOT-23-ODYCDWI CKT-25-KCJYKYL O-EPPFLWM 8-ILKLAUIFLIISTDQQQ......VINIKKLAMGGPQKYNAKANR-41 gh-h---K CPX PAND 5-YVRYADDILIGVLGSKA-2-KIIKRDLNNFLNS, LGLTINEE 4-IYQYMDDLYVGSHLEIG-1-HRTKIRELRQHLLRWGLTFDR -16-HLIYMDDIKLYAKNDKE-0-MKKLIDTTTIFSNDISMQPGLD PLLITYCENN-0-AVLFIEKLINVSREN पपपानिपर--५ al S.c.(groupII)-55-YVRYAD -14-LMRLT telomerase p123 L8543.12 YAM Dong (LINE) Consensus HIV-RT

telomerase p43 human La Xenopus LaA Drosophila La S. c. Lhplp LQKQ1EFYSSDANLYNDSFLRKLVLKSGEQRVEIETLLM ICHQLEYYFGDFNLPRDKFLKEQI.KLDEGWVPLEIMIK ICEQIEYYFGDHNLPRDKFLKQQI.LLDDGWVPLETMIK ILRQVEYYFGDANLNRDKFLREQIGKNEDGWVPLSVLVT CLKOMEFYESEFNFPYDRFLRTTAEK.NDGWVPISTIAT

1	aactcatta attactaatt taatcaacaa gattgataaa aagcagtaaa taaaacccaa
6 l	tagatttaat ttagaaagta tcaattgaaa aatggaaatt gaaaacaact aagcacaata
121	gccaaaagcc gaaaaattgt ggtgggaact tgaattagag atgcaagaaa accaaaatga
181	tatataagtt agggttaaga ttgacgatcc taagcaatat ctcgtgaacg tcactgcagc
241	atgtttgttg taggaaggta gttactacta agataaagat gaaagaagat atatcatcac
301	taaagcactt cttgaggtgg ctgagtctga tcctgagttc atctgctagt tggcagtcta
361	catccgtaat gaactttaca tcagaactac cactaactac attgtagcat tttgtgttgt
421	ccacaagaat actcaaccat tcatcgaaaa gtacttcaac aaagcagtac ttttgcctaa
	tgacttactg gaagtctgtg aatttgcata ggttctctat atttttgatg caactgaatt
541	caaaaatttg tatcttgata ggatactttc ataagatatt cgtaaggaac tcactttccg
601	taagtgttta caaagatgcg tcagaagcaa gttttctgaa ttcaacgaat actaacttgg
661	taagtattgc actgaatcct aacgtaagaa aacaatgttc cgttacctct cagttaccaa
721	caagtaaaag tgggattaaa ctaagaagaa gagaaaagag aatctcttaa ccaaacttta
781	ggcaataaag gaatetgaag ataagtecaa gagagaaact ggagacataa tgaacgttga
841	agatgcaatc aaggctttaa aaccagcagt tatgaagaaa atagccaaga gatagaatgc
901	catgaagaaa cacatgaagg cacctaaaat tcctaactct accttggaat caaagtactt
	gaccttcaag gatctcatta agttctgcca tatttctgag cctaaagaaa gagtctataa
1021	gateettggt aaaaaatace etaagacega agaggaatae aaageageet ttggtgatte
1081	tgcatctgca ccettcaate etgaattgge tggaaagegt atgaagattg aaatetetaa
1141	aacatgggaa aatgaactca gtgcaaaagg caacactgct gaggtttggg ataatttaat
1201	ttcaagcaat taactcccat atatggccat gttacgtaac ttgtctaaca tcttaaaagc
1261	cggtgtttca gatactacac actctattgt gatcaacaag atttgtgagc ccaaggccgt
1321	tgagaactee aagatgttee etetteaatt etttagtgee attgaagetg ttaatgaage
1381	agttactaag ggattcaagg ccaagaagag agaaaatatg aatcttaaag gtcaaatcga
1441	agcagtaaag gaagttgttg aaaaaaccga tgaagagaag aaagatatgg agttggagta
	aaccgaagaa ggagaatttg ttaaagtcaa cgaaggaatt ggcaagcaat acattaactc
1561	cattgaactt gcaatcaaga tagcagttaa caagaattta gatgaaatca-aaggacacac
	tgcaatcttc tctgatgttt ctggttctat gagtacctca atgtcaggtg gagccaagaa
1681	gtatggttcc gttcgtactt gtctcgagtg tgcattagtc cttggtttga tggtaaaata
	acgttgtgaa aagteeteat tetacatett eagtteacet agtteteaat geaataagtg
1801	ttacttagaa gttgatetee etggagaega acteegteet tetatgtaaa aaettttgea
	agagaaagga aaacttggtg gtggtactga tttcccctat gagtgcattg atgaatggac
	aaagaataaa actcacgtag acaatatcgt tattttgtct gatatgatga ttgcagaagg
1981	atattcagat atcaatgtta gaggcagttc cattgttaac agcatcaaaa agtacaagga
204	tgaagtaaat cctaacatta aaatctttgc agttgactta gaaggttacg gaaagtgcct
	taatctaggt gatgagttca atgaaaacaa ctacatcaag atattcggta tgagcgattc
	aatcttaaag ttcatttcag ccaagcaagg aggagcaaat atggtcgaag ttatcaaaaa
	ctttgccctt caaaaaatag gacaaaagtg agtttcttga gattcttcta taacaaaaat
	ctcaccccac ttttttgttt tattgcatag ccattatgaa atttaaatta ttatctattt
234	atttaagtta ettacatagt ttatgtateg eagtetatta geetatteaa atgattetge
240	l aaagaacaaa aaagattaaa a

MEIENNQAQQPKAEKLWWELELEMQENQNDIQVRVKIDDPKQYL

VNVTAACLLQEGSYYQDKDERRYIITKALLEVAESDPEFICQLAVYIRNELYIRTTTN

YIVAFCVVHKNTQPFIEKYFNKAVLLPNDLLEVCEFAQVLYIFDATEFKNLYLDRILS

QDIRKELTFRKCLQRCVRSKFSEFNEYQLGKYCTESQRKKTMFRYLSVTNKQKWDQTK

KKRKENLLTKLQAIKESEDKSKRETGDIMNVEDAIKALKPAVMKKIAKRQNAMKKHMK

APKIPNSTLESKYLTFKDLIKFCHISEPKERVYKILGKKYPKTEEEYKAAFGDSASAP

FNPELAGKRMKIEISKTWENELSAKGNTAEVWDNLISSNQLPYMAMLRNLSNILKAGV

SDTTHSIVINKICEPKAVENSKMFPLQFFSAIEAVNEAVTKGFKAKKRENMNLKGQIE

AVKEVVEKTDEEKKDMELEQTEEGEFVKVNEGIGKQYINSIELAIKIAVNKNLDEIKG

HTAIFSDVSGSMSTSMSGGAKKYGSVRTCLECALVLGLMVKQRCEKSSFYIFSSPSSQ

CNKCYLEVDLPGDELRPSMQKLLQEKGKLGGGTDFPYECIDEWTKNKTHVDNIVILSD

MMIAEGYSDINVRGSSIVNSIKKYKDEVNPNIKIFAVDLEGYGKCLNLGDEFNENNYI

KIFGMSDSILKFISAKQGGANMVEVIKNFALQKIGQK

l tcaatactat taattaataa ataaaaaaaa gcaaactaca aagaaaatgt caaggcgtaa 61 ctaaaaaaag ccataggctc ctataggcaa tgaaacaaat cttgattttg tattacaaaa 121 tetagaagtt tacaaaagee agattgagea ttataagaee tagtagtaat agateaaaga 181 ggaggatete aagettttaa agtteaaaaa ttaagattag gatggaaact etggeaacga 241 tgatgatgat gaagaaaaca actcaaataa ataataagaa ttattaagga gagtcaatta 301 gattaagtag caagtttaat tgataaaaaa agttggttct aaggtagaga aagatttgaa 361 tttgaacgaa gatgaaaaca aaaagaatgg actttctgaa tagcaagtga aagaagagta 421 attaagaacg attactgaag aataggttaa gtattaaaat ttagtattta acatggacta 481 ccagttagat ttaaatgaga gtggtggcca tagaagacac agaagagaaa cagattatga 541 tactgaaaaa tggtttgaaa tatctcatga ccaaaaaaat tatgtatcaa tttacgccaa 601 ctaaaagaca tcatattgtt ggtggcttaa agattatttt aataaaaaca attatgatca 661 tettaatgta ageattaaca gaetagaaac tgaageegaa ttetatgeet ttgatgattt 721 ttcacaaaca atcaaactta ctaataattc ttactagact gttaacatag acgttaattt 781 tgataataat ctctgtatac tcgcattgct tagattttta ttatcactag aaagattcaa 841 tattttgaat ataagatett ettatacaag aaattaatat aattttgaga aaattggtga 901 getacttgaa actatetteg eagttgtett tteteatege eaettacaag geatteattt 961 acaagtteet tgegaagegt tetaatattt agttaaetee teateataaa ttagegttaa 1021 agatagetaa ttataggtat actetttete tacagaetta aaattagttg acactaacaa 1081 agtccaagat tattttaagt tettataaga atteeetegt ttgactcatg taagetagta 1141 ggctatccca gttagtgcta ctaacgctgt agagaacctc aatgttttac ttaaaaaggt 1201 caagcatgct aatcttaatt tagtttctat ccctacctaa ttcaattttg atttctactt 1261 tgttaattta taacatttga aattagagtt tggattagaa ccaaatattt tgacaaaaca 1321 aaagettgaa aatetaettt tgagtataaa ataateaaaa aatettaaat ttttaagatt 1381 aaacttttac acctacgttg cttaagaaac ctccagaaaa cagatattaa aacaagctac 1441 aacaatcaaa aatctcaaaa acaataaaaa tcaagaagaa actcctgaaa ctaaagatga 1501 aactccaagc gaaagcacaa gtggtatgaa attttttgat catctttctg aattaaccga 1561 gettgaagat tteagegtta aettgtaage taeceaagaa atttatgata gettgeacaa 1621 acttttgatt agatcaacaa atttaaagaa gttcaaatta agttacaaat atgaaatgga 1681 aaagagtaaa atggatacat tcatagatct taagaatatt tatgaaacct taaacaatct 1741 taaaagatgc tetgttaata tatcaaatec teatggaaac atttettatg aactgacaaa 1801 taaagattet aetttttata aatttaaget gaeettaaae taagaattat aacaegetaa 1861 gtatactttt aagtagaacg aattttaatt taataacgtt aaaagtgcaa-aaattgaatc 1921 tteeteatta gaaagettag aagatattga tagtetttge aaatetattg ettettgtaa 1981 aaatttacaa aatgttaata ttatcgccag tttgctctat cccaacaata tttagaaaaa 2041 teettteaat aageeeaate ttetatttt caageaattt gaataattga aaaatttgga 2101 aaatgtatet ateaaetgta ttettgatea geatataett aattetattt eagaattett 2161 agaaaagaat aaaaaaataa aagcattcat tttgaaaaga tattatttat tacaatatta 2221 tettgattat aetaaattat ttaaaacaet teaatagtta eetgaattaa attaagttta 2281 cattaattag caattagaag aattgactgt gagtgaagta cataagtaag tatgggaaaa 2341 ccacaagcaa aaagctttct atgaaccatt atgtgagttt atcaaagaat catcctaaac 2401 cetttageta atagattttg accaaaacae tgtaagtgat gaetetatta aaaagatttt 2461 agaatetata tetgagteta agtateatea ttatttgaga ttgaaceeta gttaatetag 2521 cagtttaatt aaatetgaaa acgaagaaat ttaagaactt ctcaaagctt gcgacgaaaa 2581 aggtgtttta gtaaaagcat actataaatt ccctctatgt ttaccaactg gtacttatta 2701 tgaatattic tttgcttatt atttgaataa tacatacaat agtcattttt agtgttttga 2761 atatatttta gttatttaat tcattatttt aagtaaataa ttatttttca atcatttttt 2821 aaaaaaatcg

MSRRNQKKPQAPIGNETNLDFVLQNLEVYKSQIEHYKTQQQQIK EEDLKLLKFKNQDQDGNSGNDDDDEENNSNKQQELLRRVNQIKQQVQLIKKVGSKVEK DLNLNEDENKKNGLSEQQVKEEQLRTITEEQVKYQNLVFNMDYQLDLNESGGHRRHRR ETDYDTEK WFEISHDQKNYVSIYANQKTSYCWWLKDYFNKNNYDHLNVSINRLETEAE FYAFDDFSQTIKLTNNSYQTVNIDVNFDNNLCILALLRFLLSLERFNILNIRSSYTRN OYNFEKIGELLETIFAVVFSHRHLQGIHLQVPCEAFQYLVNSSSQISVKDSQLQVYSF STDLKLVDTNKVQDYFKFLQEFPRLTHVSQQAIPVSATNAVENLNVLLKKVKHANLNL VSIPTOFNFDFYFVNLQHLKLEFGLEPNILTKQKLENLLLSIKQSKNLKFLRLNFYTY VAOETSRKOILKOATTIKNLKNNKNQEETPETKDETPSESTSGMKFFDHLSELTELED FSVNLQATQEIYDSLHKLLIRSTNLKKFKLSYKYEMEKSKMDTFIDLKNIYETLNNLK RCSVNISNPHGNISYELTNKDSTFYKFKLTLNQELQHAKYTFKQNEFQFNNVKSAKIE SSSLESLEDIDSLCKSIASCKNLQNVNIIASLLYPNNIQKNPFNKPNLLFFKQFEQLK NLENVSINCILDQHILNSISEFLEKNKKIKAFILKRYYLLQYYLDYTKLFKTLQQLPE LNQVYINQQLEELTVSEVHKQVWENHKQKAFYEPLCEFIKESSQTLQLIDFDQNTVSD DSIKKILESISESKYHHYLRLNPSQSSSLIKSENEEIQELLKACDEKGVLVKAYYKFP **LCLPTGTYYDYNSDRW** 

MKILFEFIQDKLDIDLQTNSTYKENLKCGHFNGLDEILTTCFAL PNSRKIALPCLPGDLSHKAVIDHCIIYLLTGELYNNVLTFGYKIARNEDVNNSLFCHS ANVNVTLLKGAAWKMFHSLVGTYAFVDLLINYTVIQFNGQFFTQIVGNRCNEPHLPPK WVQRSSSSATAAQIKQLTEPVTNKQFLHKLNINSSSFFPYSKILPSSSSIKKLTDLR EAIFPTNLVKIPQRLKVRINLTLQKLLKRHKRLNYVSILNSICPPLEGTVLDLSHLSR OSPKERVLKFIIVILOKLLPQEMFGSKKNKGKIIKNLNLLLSLPLNGYLPFDSLLKKL RLKDFRWLFISDIWFTKHNFENLNQLAICFISWLFRQLIPKIIQTFFYCTEISSTVTI VYFRHDTWNKLITPFIVEYFKTYLVENNVCRNHNSYTLSNFNHSKMRIIPKKSNNEFR IIAIPCRGADEEEFTIYKENHKNAIQPTQKILEYLRNKRPTSFTKIYSPTQIADRIKE FKORLLKKFNNVLPELYFMKFDVKSCYDSIPRMECMRILKDALKNENGFFVRSQYFFN TNTGVLKLFNVVNASRVPKPYELYIDNVRTVHLSNQDVINVVEMEIFKTALWVEDKCY IREDGLFQGSSLSAPIVDLVYDDLLEFYSEFKASPSQDTLILKLADDFLIISTDQQQV INIKKLAMGGFQKYNAKANRDKILAVSSQSDDDTVIQFCAMHIFVKELEVWKHSSTMN NFHIRSKSSKGIFRSLIALFNTRISYKTIDTNLNSTNTVLMQIDHVVKNISECYKSAF KDLSINVTQNMQFHSFLQRIIEMTVSGCPITKCDPLIEYEVRFTILNGFLESLSSNTS KFKDNIILLRKEIQHLQAYIYIYIHIVN

Oxytricha Euplotes LCVSYILSSFYYANLEENALQFLRKESMDPEKPETNLLMRLT LCVSSILSSFYYATLEESSLGFLRDESMNPENPNVNLLMRLT

	ı
human tez1 EST2 p123	Motif 0  AKFLHWLMSVYVVELLRSFFYVTETTFQKNR  ISEIEWLVLGKRSNAKMCLSDFEKRKQIFAEFIYWLYNSFIIPILQSFFYITESSDLRNR LKDFRWLFISDIWFTKHNFENLNQLAICFISWLPRQLIPKIIQTFFYCTEISSTVT- TREISWMQVET-SAKHPYYFDHEN-IYVLWKLLRWIFEDLVVSLIRCFFYVTEQQKSYSK
human tezl EST2 Dp123	Hotif 1  LFFYRKSVWSKLQSIGIRQHLKRVQLRDVSEAEVRQHREARPALLTSRLRFIPKPDGL  TVYFRKDIWKLLCRPPI-TSMKMEAFEKINENNVRMDTQK-TTLPPAVIRLLPKKNTF  IVYFRHDTWNKLITPFIVEYFKTYLVENNVCRNHNSYTLSNFNHSKMRIIPKKSNNEF  TYYYRKNIWDVIMKMSI-ADLKKETLAEVQEKEVBEWKKS-LGFAPGKLRLIPKKTTF
Thuman tez1 E8T2 p123	Hotif 2  RPIVNMDYVVGARTFRREKRAERLTSRVKALF-SVLNYERA  RLITN-LRKRFLIKMGSNKKMLVSTNQTLRPVASILKHLINEESSGIPFNLEVYMKLLTF  RIIAIPCRGADEEEFTIYKENHKNAIQPTQKILEYLRNKRPTSFTKIYSPTQIADRIKEF  RPINTFNKKIVNSDRKTTKLTTNTKLLNSHLMLKTLKN-RMFKDPPGPAVFNYDDVMKKY  * * * * * * * * * * * * * * * * * * *
tezi EST2 p123	Motif 3 (A)  KKDLLKHRMFGR-KKYFVRIDIKSCYDRIKQDLMFRIVKK-KLKDPEPVIRKYATIHATS  KQRLLKKFNNVLPELYFMKFDVKSCYDSIPRMECMRILKD-ALKNENGFFVRSQYFFNTN  EBFVCKHKQVGQPKLPFATHDIEKCYDSVNREKLSTFLKTTKLLSSDFWIHTAQILKRKN

ATTTATACTCATGAAAATCTTATTCGAGTTCATTCAAGACAAGCTTGACATTGATCTACA GACCAACAGTACTTACAAAGAAAATTTAAAATGTGGTCACTTCAATGGCCTCGATGAAAT TCTAACTACGTGTTTCGCACTACCAAATTCAAGAAAAATAGCATTACCATGCCTTCCTGG TGACTTAAGCCACAAAGCAGTCATTGATCACTGCATCATTTACCTGTTGACGGGCGAATT ATACAACAACGTACTAACATTTGGCTATAAAATAGCTAGAAATGAAGATGTCAACAATAG TCTTTTTTGCCATTCTGCAAATGTTAACGTTACGTTACTGAAAGGCGCTGCTTGGAAAAT GTTCCACAGTTTGGTCGGTACATACGCATTCGTTGATTATTGATCAATTATACAGTAAT TCAATTTAATGGGCAGTTTTTCACTCAAATCGTGGGTAACAGATGTAACGAACCTCATCT GCCGCCCAAATGGGTCCAACGATCATCCTCATCATCCGCAACTGCTGCGCAAATCAAACA ACTTACAGAACCAGTGACAAATAAACAATTCTTACACAAGCTCAATATAAATTCCTCTTC TTTTTTTCCTTATAGCAAGATCCTTCCTTCATCATCATCTATCAAAAAGCTAACTGACTT GAGAGAAGCTATTTTTCCCACAAATTTGGTTAAAATTCCTCAGAGACTAAAGGTACGAAT TAATTTGACGCTGCAAAAGCTATTAAAGAGACATAAGCGTTTGAATTACGTTTCTATTTT GAATAGTATTTGCCCACCATTGGAAGGGACCGTATTGGACTTGTCGCATTTGAGTAGGCA ATCACCAAAGGAACGAGTCTTGAAATTTATCATTGTTATTTTACAGAAGTTATTACCCCA AGAAATGTTTGGCTCAAAGAAAATAAAGGAAAAATTATCAAGAATCTAAATCTTTTATT AAGTTTACCCTTAAATGGCTATTTACCATTTGATAGTTTGAAAAAAGTTAAGATTAAA GGATTTTCGGTGGTTGTTCATTTCTGATATTTTGGTTCACCAAGCACAATTTTGAAAACTT GAATCAATTGGCGATTTGTTTCATTTCCTGGCTATTTAGACAACTAATTCCCAAAATTAT ACAGACTTTTTTTTACTGCACCGAAATATCTTCTACAGTGACAATTGTTTACTTTAGACA TGATACTTGGAATAAACTTATCACCCCTTTTATCGTAGAATATTTTAAGACGTACTTAGT CGAAAACAACGTATGTAGAAACCATAATAGTTACACGTTGTCCAATTTCAATCATAGCAA AATGAGGATTATACCAAAAAAAGTAATAATGAGTTCAGGATTATTGCCATCCCATGCAG AGGGGCAGACGAAGAATTCACAATTTATAAGGAGAATCACAAAAATGCTATCCAGCC CACTCAAAAAATTTTAGAATACCTAAGAAACAAAAGGCCGACTAGTTTTACTAAAATATA TTCTCCAACGCAAATAGCTGACCGTATCAAAGAATTTAAGCAGAGACTTTTAAAGAAAATT TAATAATGTCTTACCAGAGCTTTATTTCATGAAATTTGATGTCAAATCTTGCTATGATTC CATACCAAGGATGGAATGTATGAGGATACTCAAGGATGCGCTAAAAAAATGAAAATGGGTT TTTCGTTAGATCTCAATATTTCTTCAATACCAATACAGGTGTATTGAAGTTATTTAATGT TGTTAACGCTAGCAGAGTACCAAAACCTTATGAGCTATACATAGATAATGTGAGGACGGT TCATTTATCAAATCAGGATGTTATAAACGTTGTAGAGATGGAAATATTTAAAACAGCTTT GTGGGTTGAAGATAAGTGCTACATTAGAGAAGATGGTCTTTTTCAGGGCTCTAGTTTATC TGCTCCGATCGTTGATTTGGTGTATGACGATCTTCTGGAGTTTTATAGCGAGTTTAAAAGC CAGTCCTAGCCAGGACACATTAATTTTAAAACTGGCTGACGATTTCCTTATAATATCAAC AGACCAACAGCAAGTGATCAATATCAAAAAGCTTGCCATGGGCGGATTTCAAAAATATAA TGCGAAAGCCAATAGAGACAAAATTTTAGCCGTAAGCTCCCAATCAGATGATGATACGGT TATTCAATTTTGTGCAATGCACATATTTGTTAAAGAATTGGAAGTTTGGAAACATTCAAG CACAATGAATAATTTCCATATCCGTTCGAAATCTAGTAAAGGGATATTTCGAAGTTTAAT AGCGCTGTTTAACACTAGAATCTCTTATAAAACAATTGACACAAATTTAAATTCAACAAA CACCGTTCTCATGCAAATTGATCATGTTGTAAAGAACATTTCGGAATGTTATAAATCTGC TTTTAAGGATCTATCAATTAATGTTACGCAAAATATGCAATTTCATTCGTTCTTACAACG CATCATTGAAATGACAGTCAGCGGTTGTCCAATTACGAAATGTGATCCTTTAATCGAGTA TGAGGTACGATTCACCATATTGAATGGATTTTTGGAAAGCCTATCTTCAAACACATCAAA ATTTAAAGATAATATCATTCTTTTGAGAAAGGAAATTCAACACTTGCAAGC

AKFLHWLMSVYVVELLRSFFYVTETTFQKNRLFFYRKSVWSKLQSIGIRQHLKR VQLRDVSEAEVRQHREARPALLTSRLRFIPKPDGLRPIVNMDYVVGARTFRREKR AERLTSRVKALFSVLNYERA

GCCAAGTTCCTGCACTGGCTGATGAGTGTGTACGTCGTCGAGCTGCTCAGGTC
TTTCTTTTATGTCACGGAGACCACGTTTCAAAAGAACAGGCTCTTTTTCTACC
GGAAGAGTGTCTGGAGCAAGTTGCAAAGCATTGGAATCAGACAGCACTTGAA
GAGGGTGCAGCTGCGGGACGTGTCGGAAGCAGAGGTCAGGCAGCATCGGGA
AGCCAGGCCCGCCCTGCTGACGTCCAGACTCCGCTTCATCCCCAAGCCTGACG
GGCTGCGGCCGATTGTGAACATGGACTACGTCGTGGGAGCCAGAACGTTCCG
CAGAGAAAAGAGGGCCCGAGCGTCTCACCTCGAGGGTGAAGGCACTGTTCAGC
GTGCTCAACTACGAGCGGCGCG



MTEHHTPKSRILRFLENQYVYLCTLNDYVQLVLRGSPASSYSNICERLRSDVQTSFSIFLHSTVVGF DSKPDEGVQFSSPKCSQSELIANVVKQMFDESFERRNILIMKGFSMNHEDFRAMHVNGVQNDLV STFPNYLISILESKNWQLLLEIIGSDAMHYLLSKGSIFEALPNDNYLQISGIPLFKNNVFEETVSKKRK RTIETSITQNKSARKEVSWNSISISRFSIFYRSSYKKFKQDLYFNLHSICDRNTVHMWLQWIFPRQFG LINAFQVKQLHKVIPLVSQSTVVPKRLLKVYPLIEQTAKRLHRISLSKVYNHYCPYIDTHDDEKILS YSLKPNQVFAFLRSILVRVFPKLIWGNQRIFEIILKDLETFLKLSRYESFSLHYLMSNIKISEIEWLVL GKRSNAKMCLSDFEKRKQIFAEFIYWLYNSFIIPILQSFFYITESSDLRNRTVYFRKDIWKLLCRPFIT SMKMEAFEKINENNVRMDTQKTTLPPAVIRLLPKKNTFRLITNLRKRFLIKMGSNKKMLVSTNQT LRPVASILKHLINEESSGIPFNLEVYMKLLTFKKDLLKHRMFGRKKYFVRIDIKSCYDRIKQDLMFR IVKKKLKDPEFVIRKYATIHATSDRATKNFVSEAFSYFDMVPFEKVVQLLSMKTSDTLFVDFVDY WTKSSSEIFKMLKEHLSGHIVKIGNSQYLQKVGIPQGSILSSFLCHFYMEDLIDEYLSFTKKKGSVL LRVVDDFLFITVNKKDAKKFLNLSLRGFEKHNFSTSLEKTVINFENSNGINNTFFNESKKRMPFFG FSVNMRSLDTLLACPKIDEALFNSTSVELTKHMGKSFFYKILRSSLASFAQVFIDITHNSKFNSCCNI YRLGYSMCMRAQAYLKRMKDIFIPQRMFITDLLNVIGRKIWKKLAEILGYTSRRFLSSAEVKWLFC LGMRDGLKPSFKYHPCFEQLIYQFQSLTDLIKPLRPVLRQVLFLHRRIAD

ggtaccgatttactttccttcataagctaattgcttcctcgaacgctcctaaatctctggaaatatttttacaagaactcaataacaataccaagtcaaattccaatatgaaggaactcaataccaagtcaaattccaatatgaaggaactcaatattttacaagaactcaataacaataccaagtcaaattccaatatgaaggaactcaatattttacaagaactcaataacaataccaagtcaaattccaatatgaaggaactcaatattttacaagaactcaataacaataccaagtcaaattccaatatgaaggaactcaatattttacaagaactcaataacaataccaagtcaaattccaatatgaaggaactcaatatttacaagaactcaataccaagtcaaattccaatatgaaggaactcaatattccaatataccaagtcaaattccaatatgaaggaactcaatatttacaatataccaagaactcaatattccaatatgaaggaactcaatattcaatataccaagaactcaatattcaatattacaatataccaagaactcaatataccaagaactcaatataccaagaactcaatataccaagaactcaatataccaagaactcaatataccaagaactcaatataccaagaactcaatataccaagaactcaatataccaagaactcaatataccaagaactcaatataccaagaactcaataccaagaactcaataccaagaactcaatataccaagaactcaaaactcaagaactcaaactcaagaactcaaactcaagaactcaaactcaagaactcaaactcaagaactcaaactcaagaactcaaactcaactcaagaactcaaactcaggttcgcttacttttaatcgtggtactgttttagctgctacttctagccaaccgcgtgtttctaccccgtcattggatatagctcttggagtagctcacagaaatccttacaaatctt ctgatgagactatattagattcattacagtccgtgcatattcttaacatggagccttacactttagatgagtcacgtcgcatgatggagtatttggtatcatccaacgtttgccttg ctcctttaacgcggttttatttttctattttctattctcatgttgttccaaatatgtatcatctcgtattaggcttttttccgttttactcctggaatcgtacctttttcactatttccccctaatg GACCGAACACCATACCCCCAAAAGCAGGATTCTTCGCTTTCTAGAGAATCAATATGTATACCTATGTA CCTTAAATGATTATGTACAACTTGTTTTGAGAGGGTCGCCGGCAAGCTCGTATAGCAATATATGCGAA CGCTTGAGAAGCGATGTACAAACGTCCTTTTCTATTTTTCTTCATTCGACTGTAGTCGGCTTCGACAGT AAGCCAGATGAAGGTGTTCAATTTTCTTCTCCAAAATGCTCACAGTCAGAGgtatatatatttttgtttttgatttttttctattcg ggatagctaatatatgggcagCTAATAGCGAATGTTGTAAAACAGATGTTCGATGAAAGTTTTGAGCGTCGAAGGA TCATGAAGATTTTCGAGCCATGCATGTAAACGGAGTACAAAATGATCTCGTTTCTACTTTTCCTAATTA CCTTATATCTATACTTGAGTCAAAAAATTGGCAACTTTTGTTAGAAATgtaaataccggttaagatgttgcgcactttgaaca agactgacaagtatagTATCGGCAGTGATGCCATGCATTACTTATTATCCAAAGGAAGTATTTTTGAGGCTCTTC CAAATGACAATTACCTTCAGATTTCTGGCATACCACTTTTTAAAAATAATGTGTTTGAGGAAACTGTGT CAAAAAAAAGCGCAACCATTGAAACATCCATTACTCAAAATAAAAGCGCCCGCAAAGAAGTTTC CTGGAATAGCATTTCAATTAGTAGGTTTAGCATTTTTTACAGGTCATCCTATAAGAAGTTTAAGCAAGgt aactaatactgttatccttcataactaattttagATCTATATTTTAACTTACACTCTATTTGTGATCGGAACACAGTACACATG TGGCTTCAATGGATTTTTCCAAGGCAATTTGGACTTATAAACGCATTTCAAGTGAAGCAATTGCACAA AGTGATTCCACTGGTATCACAGAGTACAGTTGTGCCCAAACGTCTCCTAAAGGTATACCCTTTAATTGA ACAAACAGCAAAGCGACTCCATCGTATTTCTCTATCAAAAGTTTACAACCATTATTGCCCATATATTGA CACCCACGATGATGAAAAAATCCTTAGTTATTCCTTAAAGCCGAACCAGGTGTTTGCGTTTCTTCGATC CATTCTTGTTCGAGTGTTTCCTAAATTAATCTGGGGTAACCAAAGGATATTTGAGATAATATTAAAAGg ATTATTAATGAGTAACATAAAGgtaatatgccaaattttttaccattaattaacaatcagATTTCAGAAATTGAATGGCTAGT AAGTGATTTACGAAATCGAACTGTTTATTTTAGAAAAGATATTTGGAAACTCTTGTGCCGACCCTTTAT TACATCAATGAAAATGGAAGCGTTTGAAAAAATAAACGAGgtattttaaagtattttttgcaaaaagctaatatttcagAACAA TGTTAGGATGGATACTCAGAAAACTACTTTGCCTCCAGCAGTTATTCGTCTATTACCTAAGAAGAATAC CTTTCGTCTCATTACGAATTTAAGAAAAAGATTCTTAATAAAGgtattaatttttggtcatcaatgtactttacttctaatctattattag cagATGGGTTCAAACAAAAAATGTTAGTCAGTACGAACCAAACTTTACGACCTGTGGCATCGATACTG AAACATTTAATCAATGAAGAAAGTAGTGGTATTCCATTTAACTTGGAGGTTTACATGAAGCTTCTTACT TTTAAGAAGGATCTTCTTAAGCACCGAATGTTTGGgtaattataatgcgcgattcctcattattaattttgcagGCGTAAGAAG TATTTTGTACGGATAGATATAAAATCCTGTTATGATCGAATAAAGCAAGATTTGATGTTTCGGATTGTT AAAAAGAAACTCAAGGATCCCGAATTTGTAATTCGAAAGTATGCAACCATACATGCAACAAGTGACCG AGCTACAAAAAACTTTGTTAGTGAGGCGTTTTCCTATTgtaagtttatttttcattggaattttttaacaaattctttttagTTGATAT GGATTATTGGACCAAAAGTTCTTCTGAAATTTTTAAAATGCTCAAGGAACATCTCTCTGGACACATTGT TAAGgtataccaattgttgaattgtaataacactaatgaaactagATAGGAAATTCTCAATACCTTCAAAAAGTTGGTATCCCTCTACGAAAAAGAAAGAATCAGTGTTGTTACGAGTAGTCGACGATTTCCTCTTTATAACAGTTAATAAAA ACACATTTTTCTACGAGCCTGGAGAAAACAGTAATAAACTTTGAAAATAGTAATGGGATAATAAACA ATACTTTTTTAATGAAAGCAAGAAAAGAATGCCATTCTTCGGTTTCTCTGTGAACATGAGGTCTCTTG ATACATTGTTAGCATGTCCTAAAATTGATGAAGCCTTATTTAACTCTACATCTGTAGAGCTGACGAAAC ATATGGGGAAATCTTTTTTACAAAATTCTAAGgtatactgtgtaactgaataatagctgacaaataatcagATCGAGCCTTGC ATTTGGAAAAGTTGGCCGAAATATTAGGATATACGAGTAGGCGTTTCTTGTCCTCTGCAGAAGTCAA

### FIGURE 30 (cont.)

EST2 pep	FFYCTEISST VTIVYFRHDT WNKLIT PFIVE YFK-TYLVEN	40
Euplotes pep	FFYVTEQQKS YSKTYYYRKN IWDVI-MKMS LADLKK ETLAEVQE	43
Trans of tetrahymen	KHKE GSQIFYYRKP IWKLVSKLTI VKVRIQFSEK NKQMKNNFYQ	44
Consensus	FFY.TEKSYYYRK. IWKLFKV	50
ECEC	NVCRNHNSY TLSNFNHSKY FINTEKKSNNE FRITIAIPCRG	79
EST2 pep Euplotes pep	KEVEEWKKSLGFAPCKE FULLPKKIT FREIMTFNKK	78
Trans of tetrahymen	KIQLEEENLE KVEEKLIPED SFOKYPOCKE BUTPKKGS FREIMTFLRK	92
mans of cectaryman	K. E F. CKE FINITEKK ERRIMTF.RK	100
Consensus	KE	100
	Flier appropriate programmer of the programmer o	129
EST2 pep .	ADEEDFTIYK ENHKNAIOPT OKILEYERIK RPTSFTKIYS PTOLADRIKE	
Euplotes pep	IVNSDRKTTK LTINTKLING HLMLKTIKNRMFK -DPFGFAVFN	120
Trans of tetrahymen	DKQKNIK LNLNQILMDS OLVFRATEDML-G -QKIGYSVFD	130
Consensus	K.KLN.N.L.SQL.L.LKN GVF	150
EST2 pep	FKORLLAKEN NVL FERFEMENT VKSCYD	157
Euplotes pep	YD-DVMKKYE EFVCKWKQVG GENTFFATMD TEKCYD	155
Trans of tetrahymen	NK-QISEKFA QFIEKWINKG RECEYYVTL	158
	K KWK G . LELLYF .T.D CYD	186
Consensus	KKEFFKWKG .EE.LEEF.I.DCID	100

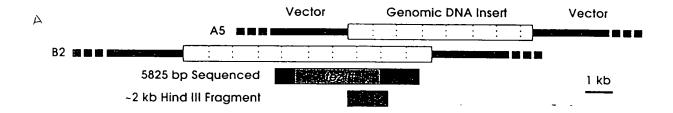
S-1: FFY VTE TTF QKN RLF FYR KSV WSK

S-2: ROH LKR VOL RDV SEA EVR OHR EA S-3: ART FRR EKR AER LTS RVK ALF SVL NYE

A-1: AKF LHW LMS VYV VEL LRS FFY VTE TTF Q A-2: LFF YRK SVW SKL QSI GIR QHL KRV QLR DVS A-3: PAL LTS RLR FIP KPD GLR PIV NMD YVV

B

#### FIGURE 33



tez1+ **RT Motifs** 12 3(A) 4(B') 5(C) 6(D) Introns 2 B \$6 789 10 11 12 13 14 15 Hind III Xca Xca I Hind III Original PCR 3' RT-PCR 4-1 ¢DNA 2 3 & 5-20 CDNA 5' RT-PCR w/ M2-B14 5' RT-PCR w/ M2-B15 Band A 5' RT-PCR w/ M2-B15 Band B 500 bp 5'RT-PCR w/ M2-B16 Band C

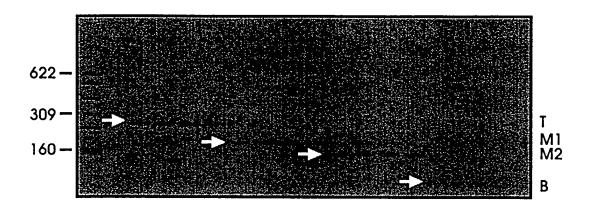
Poly 4

t t c
ta a g c c t c g
5'- cag acc aaa gga att cca taa gg -3'
Q T K G I P Q G

4 (B')

5 (c')

DDYLLIT 3'- ctg ctg atg gag gag tag tgg -5' a a a a a a a a a t t t t c c Poly 1



Motif B' (4)

QTKGIPQG

Motif C (5)

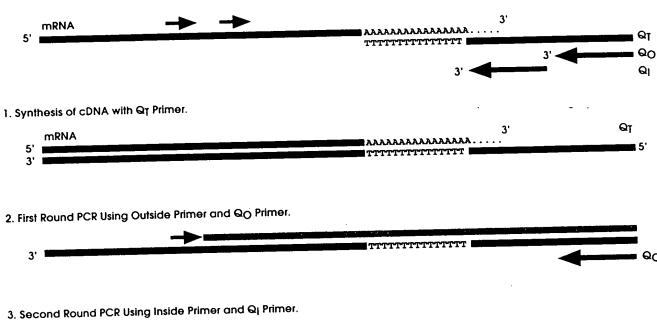
DDYLLIT

## PCR Product M2 showed Reasonable Match with Other Telomerase Proteins

```
Ot
                      LCVSYILSSFYYANLEENALQFLRKESMDPEKPETNLLMRLT
  Ea_p123
               KGIPQGLCVSSILSSFYYATLEESSLGFLRDESMNPENPNVNLLMRLTDDYLLIT
                      SILSSFLCHFYMEDLIDEYLSFTKKK-----GSVLLRVV
  Sp_M2
  Sc_p103
               DGLFQGSSLSAPIVDLVYDDLLEFYSEFKASPS-----QDTLILKLADDFLIIS
    KVGIPQG
  caa aaa gtt ggt atc cct cag gg..... <---Actual Genomic Sequence.
  Poly 4
M
Œ
              t
           g c c t c g
  cag acc aaa gga att cca taa gg ---->
   ag acc aaa gga att cca tca ggC TCA ATT CTG TCA TCT TTT TTG TGT CAT TTC TAT ATG
   tc tgg ttt cct taa ggt agt ccG AGT TAA GAC AGT AGA AAA AAC ACA GTA AAG ATA TAC
" LI II E
                       S
                           G
                               S
                                  Ι
                                     L
                                         S
                                             S
                                                    L
                                                        C
GAA GAT TTG ATT GAT GAA TAC CTA TCG TTT ACG AAA AAG AAA GGA TCA GTG TTG TTA CGA
  CTT CTA AAC TAA CTA CTT ATG GAT AGC AAA TGC TTT TTC TTT CCT AGT CAC AAC AAT GCT
                    Ε
                       Y
                           L
                               S
                                  F
                                      Т
                                         K
                                             K
                                                K G
                                                        S
  GTA GTC gac gac tac ctc ctc atc acc
  CAT CAG ctg ctg atg gag gag tag tgg
    V D
            D Y
                    L L
                           Ι
    <---- ctg ctg atg gag gag tag tgg
           a a aaaaa
                         t
                             t t
                     t
                     С
                         C
                             Poly 1
     .....gac gat ttc ctc ttt ata aca...... <---Actual Genomic Sequence.
```

DDFLFI

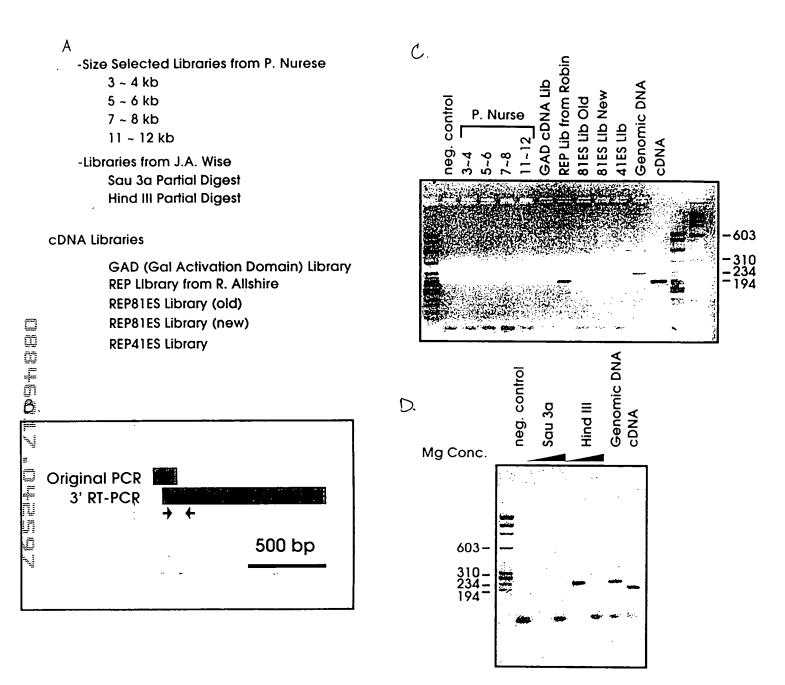
#### 3' RT PCR Strategy

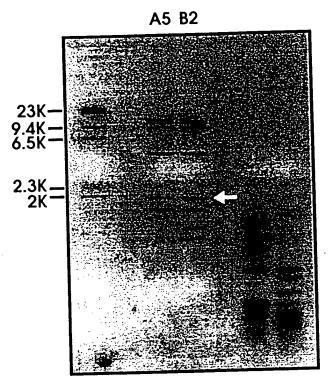




4. Sequence Second Round PCR Products Using Inside Primer or Q<sub>1</sub> Primer.



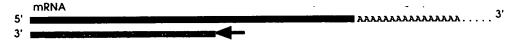




Hind III Digested Positive Genomic Clones



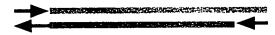
1. Synthesis of cDNA with Specific Downstream Primer.



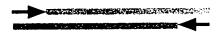
2. Ligate Oligo with 5'-P and blocked 3' to cDNA using T4 RNA Ligase.



3. First Round PCR



4. Second Round PCR



#### Alignment of RT Domains from Telomerase Catalytic Subunits.

```
Motif O
S.p. Tez1p (429). WLYNSFIIPILQSFFYITESSDLRNRTVYFRKDIW ...(35)...
S.c. Est2p (366). WLFRQLIPKIIQTFFYCTEISSTVT-IVYFRHDTW ...(35)...
           (441). WIFEDLVVSLIRCFFYVTEQQKSYSKTYYYRKNIW ...(35)...
E.a. p123
                        Motif 2
             Motif 1
                                    K
            p hh h K
                         hR h
            AVIRLLPKK--NTFRLITN-LRKRF ...(61)...
S.p. Tezlp
            SKMRIIPKKSNNEFRIIAIPCRGAD ...(62)...
S.c. Est2p
            GKLRLIPKK--TTFRPIMTFNKKIV ... (61) ...
E.a. p123
                 * * *
            Motif 3(A) AF
               h hDh GY
                           h
            KKYFVRIDIKSCYDRIKQDLMFRIVK ...(89)...
S.p. Tezlp
            ELYFMKFDVKSCYDSIPRMECMRILK ... (75) ...
S.c. Est2p
            KLFFATMDIEKCYDSVNREKLSTFLK ...(107)...
E.a. p123
             Motif 4(B')
                  hPOG
                         pP hh
                                  h
            YLQKVGIPQGSILSSFLCHFYMEDLIDEYLSF ...(6)...
S.p. Tezlp
S.c. Est2p
            YIREDGLFQGSSLSAPIVDLVYDDLLEFYSEF
            YKQTKGIPQGLCVSSILSSFYYATLEESSLGF
E.a. p123
                Y Motif 5(C)
                                              Motif 6(D)
                                              Gh h cK h
               F DDhhh
S.p. Tezlp
            VLLRVVDDFLFITVNKKDAKKFLNLSLRGFEKHNFSTSLEKTVINFENS .(205)
            LILKLADDFLIISTDQQQVINIKKLAMGGFQKYNAKANRDKILAVSSQS .(173)
S.c. Est2p
            LLMPLTDDYLLITTQENNAVLFIEKLINVSRENGFKFNMKKLQTSFPLS .(209)
E.a. p123 ~
```

A

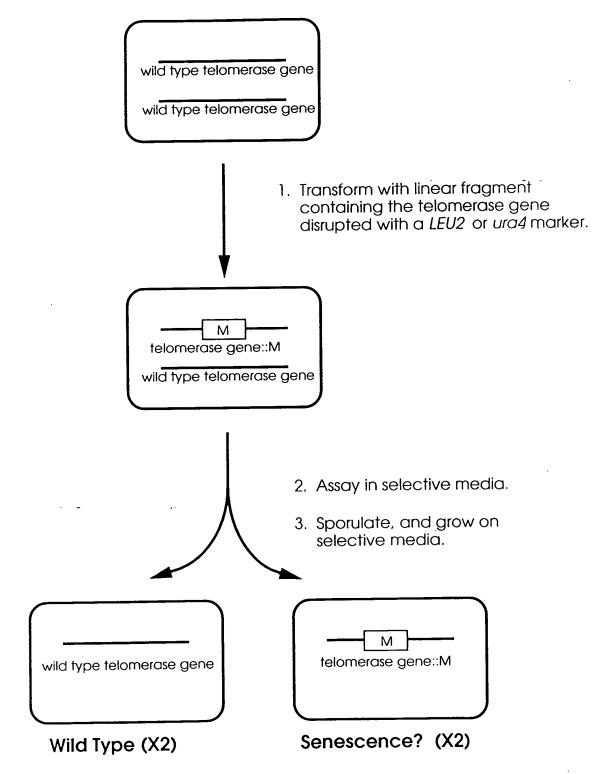
#### FIGURE 42

Sp\_TIPIP " YVKOMEDES FERRS - WKK SMNHEDFRAMM "25 Sc\_ESSP " ILVE TOELVM ... W TYKIAR ED ... " Sp\_Tip1p 300 MIK I SEE CERFY L G KR S NAK MC L SEE KR K G I FA do Sc\_Estop 300 L R L K O FR ME F I S - - - O I WI T K H H ME K L MEL A I 300 E J L R L K O FR ME S L M G V E T S - A K ME Y F FEM ME - I V V L W do S Sp. TD1P SE TENT KLECKEN TSMILLE AFEK I HANNERMOS SE SEZDO SE THAT HANNERMOS SEZDOS TO THAT HAND VINK MEN A DESTRUCTION THAT SECONDER EEE WEEK Sp.Tppp on LEKY

Sc.Est20 es IRED (LFFC S. APIVDLY DE LF SE KA est

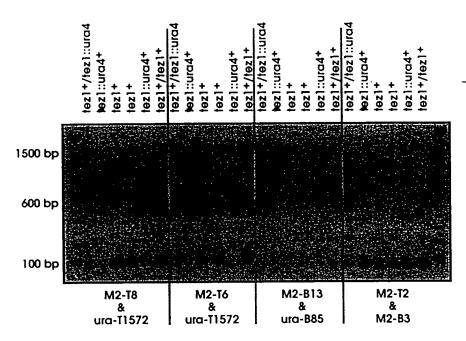
En\_D121 70 KETK SE CLCV II SS AT ELSSEQUER 70 So\_Tip1p 500 FKYHPCFEQLIYOMOSLTDLIKPLRPYMRQVLF 601
Sc\_EAZD 500 TS......KPKONIILLRKEIOHDQAYIY 577
Ea\_p123 600 IEIFS...TKKYIMINRVCMILKAKEAKMEKSDQC 1002 Sp\_Tppp === FKYHPCFEOLIMO OSLTO IMPLRPYROVLF === Sc\_Est2p === TS - - - - - - - - K KONI IMPLRYE OH OAYIY === Ep. 123 === IEIFS - - TKKMII NRYCMIM AKEAK KSOOC ==== Sp\_Tip1p sez LHRREAD -Sc\_Est2p e7s IVIKEVH -Ea\_p123 sez OSLIOYEA

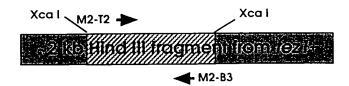
FIGURE 43
Disruption strategy for the putative telomerase genes.

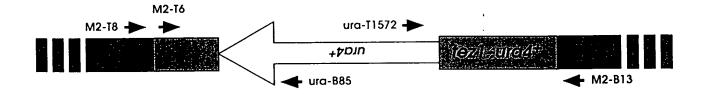


(These cells will show a senescence phenotype if the disrupted gene encodes a telomerase subunit.)

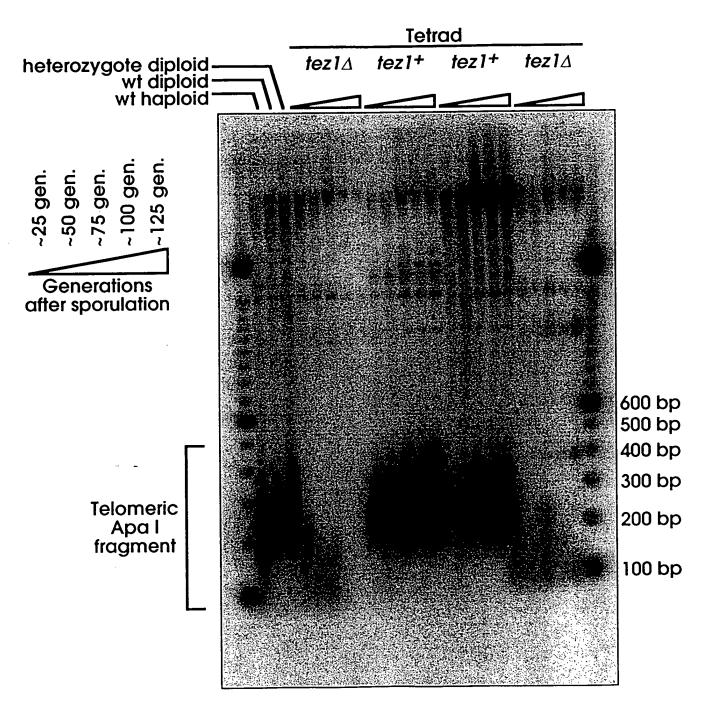
#### An Example of Confirmation of tez1 disruption By PCR







# *Tez1* disruption causes progressive shortening of telomeres in *S. pombe*



81 a 161 241 321 401 481 561 641 721 801 881	ggt ago tta gtt att cca ata gat	taa	taa gtat gct ettg ataa agat atat ettt	caat aagg tact gagt gagc ttat attc gtat aatt	acca acaa actta actta acaa acat aaaa	aagt aaaa aatc acac caaa aatt ctcg ttcg	caaagaagaagaagaatti atciitatii at	actinactinactinactinactinactinactinactin	actto actg tect atga gtec ecac gget aatt ctat	atatectt. taca gtca ttaca ttaca ttaca tcata catt agga	gaag cccc agct aatc cgtc tggt actc gtag atat cact	gtgt ctaa gcta ttct gcat ggta cttt tttt t	tatta agac cttc gatg gatg atcc aacg actc aaga aaaa	agtgatage the state of the stat	actt caac tata attt aagt ttta aatc tgat ataa agtt	ataa tatt cgcg ttag ggta tttt gtac tcta tcta	aatt tgtt atto tcat tgat tcta cttt acaat	tacta tcta atta ccaa gctt tttt ttca tgta atta	ttttc cccc cagt cgtt gcac ctat ctat atgt	eaaat egtca eccgt eccgt etctc etccc etatt aatat	atat ttgg gcat ttga ctag cctag ccta tctag tactt		240 320 400 480 560 640 720 800
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1273 87		ATA I	GCG A	AAT N	GTT V	GTA V	AAA K	CAG Q	atg M	TTC F	GAT D	GAA E	AGT S	TTT F	GAG E	CGT R	CGA R	AGG R	AAT N	CTA L	1332 106
1333 107		ATG M	AAA K	GGG G	TTT F	TCC S	ATG M	gta	aggt	attc	taat	tgtga	aaat	attt	acct	gcaa	ttac	tgtt	tcaaa	agaga	1405 113
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1662 176	ААТ	TAC Y	CTT L	CAG Q	ATT I	TCT S	GGC G	ATA I	CCA P	CTT L	TTT F	AAA K	AAT N	AAT N	GTG V	TTT F	GAG E	GAA E	ACT T	GTG V	1721 195
1722 196		AAA K	AAA K	AGA R	AAG K	CGA R	ACC T	ATT I	GAA E	ACA T	TCC S	ATT I	ACT T	CAA Q	AAT N	AAA K	AGC S	GCC A	CGC R	AAA K	1781 215
14782 = 216		GTT V	TCC S	TGG W	AAT N	AGC S	ATT I	TCA S	ATT I	AGT S	AGG R	TTT F	AGC S	ATT I	TTT F	TAC Y	AGG R	TCA S	TCC S	TAT Y	1841 235
<b>1</b> 842	AAG	AAG	ТТТ	AAG	CAA	G gt	aact	aata	actgt	tato	cctt	cataa	actaa	attt	ag A	AT CI	TA TA	AT TI	ia Ti	AC .	
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1968 266			GGA G	-								CAA Q								GTA V	2027 285
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2088 306 2148	S GCA A GAC D	Q AAG K ACC T CTT	S CGA R CAC H	T CTC L GAT D	V CAT H GAT D	V CGT R GAA E	P ATT I AAA K GTT	TCT S ATC I	R CTA L CTT L GTG	L TCA S AGT S	L AAA K TAT Y	K GTT V TCC S	V TAC Y TTA L	Y AAC N AAG K	P CAT H CCG P	L TAT Y AAC N	TGC C CAG Q AAC	E CCA P GTG V	Q TAT Y TTT F	T ATT I GCG A	305 2147 325 2207

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	2397 396	gtaa	tatg	ccaa	attt	tttt	acca	ttaa	ttaa	caat	cag	ATT I	TCA S	GAA E	ATT I	GAA E	TGG W	CTA L	GTC V	CTT L	GGA G	2465 405
	2466 406		AGG R		AAT N	GCG A	AAA K	ATG M	TGC C	TTA L	AGT S	GAT D	TTT F	GAG E	AAA K	CGC R	AAG K	CAA Q	ATA I	TTT F	GCG A	2525 425
	2526 426		TTC F	ATC I	TAC Y	TGG W	CTA L		AAT N	TCG S	TTT F	ATA I	ATA I	CCT P	ATT I	TTA L	CAA Q	TCT S	TTT F	TTT F	TAT Y	2585 445
	2586 446	ATC	ACT T	GAA E	TCA S	AGT S	GAT D	TTA L		AAT N	CGA R	ACT T	GTT V	TAT Y	TTT F	AGA R	AAA K	GAT D	ATT I	TGG W	AAA K	2645 465
	2646 466	СТС		TGC		CCC P	TTT F	ATT I	ACA T	TCA S	ATG M	AAA K	ATG M	GAA E	GCG A	TTT F	GAA E	AAA ·	-ATA I	AAC N	GAG E	2705 485
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	2968 543		TCG S	ATA I	CTG L	AAA K	CAT H	TTA L	ATC I	AAT N	GAA E	GAA E	AGT S	AGT S	GGT G	ATT I	CCA P	TTT F	AAC N	TTG L	GAG E	3027 562
	3028 563		TAC Y	ATG M	AAG K	CTT L	CTT L	ACT T	TTT F	AAG K	aag K	GAT D	CTT L	CTT L	aag K	CAC H	CGA R	ATG M	TTT F	GG G	gtaat	3088 581
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	3156 592		TCC S	TGT C	TAT Y	GAT D	CGA R	ATA I	aag K	CAA Q	GAT D	TTG L	ATG M	TTT F	CGG R	ATT I	GTT V	AAA K	aag K	AAA K	CTC L	3215 611
	3216 612		GAT D	CCC P	GAA E	TTT F	GTA V	ATT I	CGA R	AAG K	TAT Y	GCA A	ACC T	ATA I	CAT H	GCA A	ACA T	AGT S	GAC D	CGA R	GCT A	3275 631
		ACA	AAA K	AAC N	TTT F	GTT V	AGT S	GAG E	GCG A	TTT F	TCC S	TAT Y	T g	taag	ttta	tttt	ttca	ttgg	aatt	tttt	aacaa	3343 643
		att				GAT D	ATG M	GTG V	CCT P	TTT F	GAA E	AAA K	GTC V	GTG V	CAG Q	TTA L	CTT L	TCT S	atg M	AAA K	ACA T	3405 659
		TCA	GAT D	ACT T	TTG L	_		GAT D	TTT F	GTG V	GAT D	TAT Y	TGG W	ACC T	AAA K	AGT S	TCT S	TCT S	GAA E	ATT	TTT F	3465 679
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	554 729				aag K	AAA K	GGA G	TCA S	GTG V	TTG L	TTA L	CGA R	GTA V	GTC V	GAC D	GAT D	TTC F	CTC L	TTT F	ATA I	ACA T	3713 748
37		GTT	AAT N		aag K	GAT D	GCA A	AAA K	AAA K	TTT F	TTG L	AAT N	TTA L	TCT S	TTA L	AGA R	G gt	gagt	tgct	gtca	attcc	3777 764
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GCCI	AAGTT	CCTC	GCACT	'GGC'I	TG	ATG	AGT	GTG	TAC	GTC	GTC	GAG	CTG	CTC
10 arg AGG	ser TCT	phe TTC	phe TTT	tyr TAT	val GTC	thr ACG	glu GAG	thr ACC	thr ACG	20 phe TTT	gln CAA	lys AAG	asn AAC	arg AGG
leu CTC	phe TTT	phe TTC	tyr TAC	arg CGG	30 lys AAG	ser AGT	val GTC	trp TGG	ser AGC	lys AAG	leu TTG	gln CAA	ser AGC	ile ATT
40 gly GGA	ile ATC	arg AGA	gln CAG	his CAC	leu TTG	lys AAG	arg AGG	val GTG	gln CAG	50 leu CTG	arg CGG	glu GAG	leu CTG	ser TCG
glu GAA	ala GCA	glu GAG	val GTC	arg AGG	60 gln CAG	his CAT	arg CGG	glu GAA	ala GCC	arg AGG	pro CCC	ala GCC	leu CTG	leu CTG
70 thr ACG	ser TCC	arg AGA	leu CTC	arg CGC	phe TTC	ile ATC	pro CCC	lys AAG	pro CCT	80 asp GAC	gly GGG	leu CTG	arg CGG	pro CCG
ile ATT	val GTG	asn AAC	met ATG	asp GAC	90 tyr TAC	val GTC	val GTG	gly GGA	ala GCC	arg AGA	thr ACG	phe TTC	arg CGC	arg AGA
100 glu GAA	lys AAG	ARG	ala GCC	glu GAG	arg CGT	leu CTC	thr ACC	ser TCG	arg AGG	110 val GTG	lys AAG	ala GCA	leu CTG	phe TTC
ser AGC	val GTG	leu CTC	asn AAC	tyr TAC	120 glu GAG	arg CGG	ala GCG	arg CGG	arg CGC	pro CCC	gly GGC	leu CTC	leu CTG	gly GGC
130 ala GCC	ser TCT	val GTG	leu CTG	gly GGC	leu CTG	asp GAC	asp GAT	ile ATC	his CAC	140 arg AGG	ala GCC	trp TGG	arg CGC	thr ACC
phe TTC	val GTG	leu CTG	arg CGT	val GTG	150 arg CGG	ala GCC	gln CAG	asp GAC	pro CCG	pro CCG	pro CCT	glu GAG	leu CTG	tyr TAC
160 phe TTT	val GTC	lys AAG	val GTG	asp GAT	val GTG	thr ACG	gly GGC	ala GCG	tyr TAC	170 asp GAC	thr ACC	ile ATC	pro CCC	gln CAG
asp GAC	arg AGG	leu CTC	thr ACG	glu GAG	180 val GTC	ile ATC	ala GCC	ser AGC	ile ATC	ile ATC	lys AAA	pro CCC	gln CAG	asn AAC

190 thr ACG	tyr TAC	cys TGC	val GTG	arg CGT	arg CGG	tyr TAT	ala GCC	val GTG	val GTC	200 gln CAG	lys AAG	ala GCC	ala GCC	met ATG
gly GGC	thr ACG	ser TCC	ala GCA	arg AGG	210 pro CCT	ser TCA	arg AGA	ala GCC	thr ACG	ser TCC	tyr TAC	val GTC	gln CAG	cys TGC
220 gln CAG	gly GGG	ile ATC	pro CCG	gln CAG	gly GGC	ser TCC	ile ATC	leu CTC	ser TCC	230 thr ACG	leu CTG	leu CTC	cys TGC	ser AGC
leu CTG	cys TGC	tyr TAC	gly GGC	asp GAC	240 met ATG	glu GAG	asn AAC	lys AAG	leu CTG	phe TTT	ala GCG	gly GGG	ile ATT	arg CGG
250 arg CGG	asp GAC	gly GGG	leu CTG	leu CTC	leu CTG	arg CGT	leu TTG	val GTG	asp GAT	260 asp GAT	phe TTC	leu TTG	leu TTG	val GTG
thr ACA	pro CCT	his CAC	leu CTC	thr ACC	270 his CAC	ala GCG	lys AAA	thr ACC	phe TTC	leu CTC	arg AGG	thr ACC	leu CTG	val GTC
280 arg	alv	val	pro	alu	tvr	alv	cvs	val	val	290 asn	leu	arq	lys	thr ACA
val	val	asn	phe	pro	300 val	qlu	asp	qlu	ala	leu	gly	gly	thr	ala GCT
310 phe	val	aln	met	pro	ala	his	qly	leu	phe	320 pro	trp	cys	gly	leu CTG
leu	leu	asp	thr	arq	330 thr	leu	glu	val	gln	ser	asp	tyr	ser	ser AGC
340 tyr	ala	arq	thr	ser	ile	arg	ala	ser	leu	350 thr	phe	asn	arg	gly GGC
phe	lys	ala	qly	arq	360 asn	met	arg	arg	lys	leu	phe	gly	val	leu TTG
370 arg	leu	lvs	cvs	his	ser	leu	phe	leu	asp	380 leu	gln	val	asn	ser AGC



leu gln thr											
400 ala tyr arg GCG TAC AGG											
gln val trp	lys asn AAG AAC	420 pro 1 CCA	his CAT	phe TTT	ser TCC	cys TGC	ala GCG	ser TCA	ser TCT	leu CTG	thr ACA
430 arg leu pro CGG CTC CCT	leu leu CTG CTA	leu l	his CAT	pro CCT	glu GAA	ser AGC	440 gln CAA	glu GAA	arg CGC	arg AGG	asp GAT
val ala gly GTC GCT GGG	gly gln GGC CAA	450 gly a	arg CGC	arg CGC	arg CGG	pro CCC	ser TCT	ala GCC	leu CTC	arg CGA	gly GGC
460 arg ala val CGT GCA GTG	ala val GCT GTG	pro p	pro CCA	ser AGC	ile ATT	pro CCT	470 ala GCT	gln CAA	ala GCT	asp GAC	ser TCG
thr pro cys	his leu CAC CTA	480 arg a	ala GCC	thr ACT	pro CCT	gly GGG	val GTC	thr ACT	gln CAG	asp GAC	ser AGC
490 pro asp ala CCA GAC GCA											
pro gly gly	arg ser CGC AGC	510 gln j CAA	pro CCC	gly GGC	thr ACT	ala GCC	leu CTC	arg AGA	leu CTT	gln CAA	asp GAC
520 his pro gly CAT CCT GGA	leu met CTG ATG	ala GCC	thr ACC	arg CGC	pro CCA	gln CAG	530 pro CCA	gly GGC	arg CGA	glu GAG	gln CAG
thr pro ala	ala leu GCC CTG	540 ser TCA	arg CGC	arg CGG	ala GCT	tyr TAT	thr ACG	ser TCC	gln CAG	gly GGA	gly GGG
550 arg gly gly AGG GGC GGC	pro his	pro (	gly GGC	leu CTG	his CAC	arg CGC	560 trp TGG	glu GAG	ser TCT	glu GAG	ala GCC
564 OP TGA GTGAGTG	STTTGGCCG	AGGCC	TGCA	ATGTO	CCGG	CTGA	AGGC'	rgag'	rgtco	CGGC:	rgaggc
CTGAGCGAGTG	STCCAGCCA	AGGGC	TGAG	STGTO	CCAG	CACA	CCTG	CGTT	rtcac	CTTC	CCCAC







LVVSLIRCFFYVTEQQKSYSKTFIIPILQSFFYITESSDLRNRTLIPKIIQTFFYCTEISSTVTIVYVVELLRSFFYVTETTFQKNRL FFY TE
K phhh K hR h RKSLGFAPGKLRLIPKKTTFRPIMTFNKKIVQKTTLPPAVIRLLPKKNTFRLITNLRKRFLTLSNFNHSKMRIIPKKSNNEFRIIAIPCRGADARPALLTSRLRFIPKPDGLRPIVNMDYVVG R PK R I
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hPQG pS hhNGKFYKQTKGIPQGLCVSSILSSFYYAGNSQYLQKVGIPQGSILSSFLCHFYMEEDKCYIREDGLFQGSSLSAPIVDLVYDRATSYVQCQGIPQGSILSTLLCSLCYG G QG S
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KKGSVLLRVVDDFLFITVNKKD SQDTLILKLADDFLIISTDQQQ RRDGLLLRLVDDFLLVTPHLTH DD L
GhhcKNVSRENGFKFNMKKLLNLSLRGFEKHNFSTKKLAMGGFQKYNAKALRTLVRGVPEYGCVV G